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STUDIES ON HEREDITY IN JEWISH DIABETIC PATIENTS*

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THE following is a study of heredity in diabetic patients seen at the Beth Israel Hospital, since its opening in 1928. The data have been collected from the records of ward, private and outdoor patients. In addition a group of patients and their relatives has been studied as to blood types and blood groups in order to detect the relation, if any, between the diabetic constitution and the known blood characters.

For the purpose of better comparison we have used the same method of approach as Joslin and his collaborators,[1] who have collected the data of many other writers.

The importance of heredity as an etiologic factor in diabetes mellitus is now generally accepted. What is inherited, it appears, is a constitutional abnormality which predisposes the subject to diabetes, and such an individual is generally called a carrier. He may not himself develop diabetes, but transmits the predisposition to his children. Cases in which there is a diabetic parent, grandparent, uncle, aunt, nephew, niece or child are classified as hereditary; and those in which there is a diabetic brother, sister or first cousin are classified as familial. The more thorough the questioning, the higher is likely to be the recorded number of both groups. Of 1376 patients seen by various members of the hospital staff, 1037 had their family histories recorded as to the presence of diabetes; 339 made no statement as to familial history and were therefore excluded from the series. Among 1000 successive non-diabetic patients admitted to the hospital, 63 reported one or more members of their families as having had diabetes.

Table 1 illustrates the high incidence of diabetes in the families of diabetic patients. The disease is shown to be at least four times as frequent as in the families of non-diabetic subjects. According to Cammidge it is even more than eleven times as frequent. A comparison between Jewish and all diabetic patients shows only a slight difference in the incidence of heredity. More detailed studies, however, bring out a higher frequency of diabetes in the Jewish families. Cammidge and Finke found a lower incidence of diabetes (3.4 and 3.8 per cent respectively) in their mixed non-diabetic groups than we did in our Jewish non-diabetic patients (6.3 per cent) while Kern observed about the same percentage (6.2 per cent). Larger groups of Jews and non-Jews will therefore have to be studied in order to reach a definite conclusion.

TABLE 1. *Comparative Incidence of Diabetes in the Families of Diabetic and Non-Diabetic Patients.**

AUTHOR	DIABETIC PATIENTS		NON-DIABETIC PATIENTS	
	NO. OF CASES	PERCENTAGE WITH FAMILY HISTORY OF DIABETES	NO. OF CASES	PERCENTAGE WITH FAMILY HISTORY OF DIABETES
ALL PATIENTS				
Joslin et al. (Boston, 1897-1928)	6357	24.5	—	—
Cammidge (London, 1934)	1000	39.6	500	3.4
Finke (Berlin, 1925–1930)	1500	26.2	1000	3.8
Kern (Philadelphia, 1934)	300	25.3	500	6.2
JEWISH PATIENTS				
Joslin et al. (Boston, 1897–1928)	889	29.6	—	—
Rudy and Keeler (Boston, 1928–1937)	1037	29.1	1000	6.3

*Compiled from Joslin's[1] tables with the addition of our data.

Table 2 shows the incidence of diabetes in the families of Jewish diabetic patients as observed in our cases and compared with the group of mixed diabetic patients compiled by Joslin et al.[1] From the data on the hospital records we found 29.1 per cent with one or more diabetic individuals in their families. Interviews with 246 Jewish diabetic patients revealed a higher percentage of positive family histories, namely 87 (35.3 per cent). Of 302 patients with a positive family history of diabetes, 164 (15.8 per cent) gave a hereditary history, and 138 (13.3 per cent) a familial history only. Adult

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Jewish diabetic patients (age twenty and over) show 28.6 per cent diabetic heredity — 15.3 per cent hereditary and 13.3 per cent familial. Joslin's adult Jewish diabetic patients showed 29.6 per cent heredity. Table 2 shows clearly the higher incidence of diabetic heredity in Jewish patients as compared with others. The difference is in the familial type.

TABLE 2. *Comparative Incidence of Diabetes in the Families of All and Jewish Diabetic Patients.*

Author	No. of Cases	Family History of Diabetes: Hereditary*	Familial	Hereditary and Familial	Total
		%	%	%	%
All Patients					
Joslin et al. (Boston, 1897–1928)	6357	15.9	8.6	3.3	24.5
Cammidge (London, 1934)	1000	—	—	—	39.6
Mueller (Berlin, 1931–1933)	1372	—	—	—	25.4
Finke (Berlin, 1925–1930)	1500	18.7	7.5	—	26.2
Jewish Patients					
Mueller (Berlin, 1931–1933)	—	—	—	—	33.0
Finke (Berlin, 1925–1930)	—	—	—	—	55.0
Rudy and Keeler (Boston, 1928–1937)	1037	15.8	13.3	3.5	29.1
Adult Jewish Patients					
Joslin et al. (Boston, 1897–1928)	889	—	—	—	29.6
Rudy and Keeler (Boston, 1928–1937)	1015	15.3	13.3	3.2	28.6

*Hereditary consists of hereditary only and hereditary and familial cases.

also the percentage of cases reporting hereditary and familial types of family history by sex. The percentage of positive family histories for Jewish men was highest in Joslin's[1] group, namely 30.3 per cent as compared to 24.5 per cent in our male group and 23.0 per cent in all his male diabetic patients. For Jewish women he found 29.1 per cent positive family histories, while we had 30.8 per cent and those in his group of all women totaled 26.5 per cent. Jewish patients have shown a higher frequency of the familial type of diabetic heredity regardless of age. This has been equally observed in both groups. Our female Jewish diabetic patients show an especially high incidence in the total hereditary type at ages under forty-five, with a marked decrease at the ages of forty-five and over. The same phenomenon was found to a certain degree in our Jewish male diabetic patients. This may not be a significant finding, since the number of patients seen by us in the younger group was comparatively small. Joslin found that the percentage of positive family histories in his Jewish male patients was distinctly higher at the younger ages and decreased perceptibly with age. Among his Jewish women, however, the variation by age in this respect was relatively small. The incidence of hereditary-type histories at the younger ages is distinctly higher among the Jewish patients than among all patients, whereas at the older ages the reverse is true. This statement has been made by Joslin and is confirmed by our data.

TABLE 3. *Comparative Incidence of Diabetes in the Families of All and Jewish Adult Diabetic Patients in Relation to the Age and Sex of the Patient.*

Author	Ages	Family History of Diabetes — Men: No. of Cases	Hereditary*	Familial	Hereditary and Familial	Total	Women: No. of Cases	Hereditary*	Familial	Hereditary and Familial	Total
	yr.		%	%	%	%		%	%	%	%
Jewish Patients											
Rudy and Keeler (Boston, 1928–1937)	20 and over	362	13.2	11.3	2.4	24.5	653	16.5	14.3	3.6	30.8
	20–34	19	21.0	10.5	5.2	31.5	24	41.6	—	4.1	41.6
	35–44	43	25.6	2.3	2.3	27.9	84	33.3	9.5	8.3	42.8
	45–54	92	13.1	11.9	1.0	25.0	159	16.3	16.3	3.7	33.2
	55–64	112	15.1	13.4	4.4	28.5	243	12.7	15.6	2.9	28.3
	65 and over	96	4.1	12.5	1.0	16.6	143	9.0	14.6	2.1	23.9
Joslin et al. (Boston, 1897–1928)	Adult					30.3					29.1
All Patients											
Joslin et al. (Boston, 1897–1928)	20 and over	2779	14.5	8.5	2.8	23.0	2914	16.8	9.7	4.0	26.5
	20–34	401	17.2	6.0	3.0	23.2	286	17.5	5.2	4.9	22.7
	35–44	418	17.5	7.9	2.4	25.4	328	18.3	8.9	4.5	27.2
	45–54	723	17.6	8.3	2.2	25.9	791	22.6	9.5	4.0	32.1
	55–64	799	11.8	9.4	3.8	21.2	928	12.5	10.6	4.3	23.1
	65 and over	438	9.1	9.8	2.3	18.9	527	14.2	11.4	2.3	25.6

*Hereditary consists of hereditary only and hereditary and familial cases.

Table 3 shows the incidence of diabetes in the family history of adult Jewish and mixed diabetic patients in relation to the age of the patient,

The ratio of women to men is of interest (Table 4). Of 1376 patients, 487 were men and 889 women, a ratio of 1:1.8, or 82.3 per cent more

women than men. If we add their known relatives with diabetes we find that the female diabetic patients (1173) still outnumber the men (658) by 78.2 per cent. Joslin[1] found that up to the end of 1928 the number of his Jewish women patients exceeded that of men by 46.3 per cent,

TABLE 4. *Age at Onset and Sex Incidence among Jewish Diabetic Patients.*

	No. of Cases		Ratio of Men to Women	Per Cent of All Ages	
	Men	Women		Men	Women
Age at onset in years:					
Less than 20	11	9	1:0.8	4.1	2.0
20–24	4	5	1:1.2	1.5	1.1
25–29	4	5	1:1.2	1.5	1.1
30–34	10	19	1:1.9	3.7	4.2
35–39	25	27	1:1.0	9.3	6.0
40–44	30	53	1:1.7	11.2	11.8
45–49	31	76	1:2.4	11.5	16.9
50–54	44	80	1:1.8	16.4	17.8
55–59	43	70	1:1.6	16.0	15.6
60–64	27	70	1:2.6	10.1	15.6
65–69	16	19	1:1.2	5.9	4.2
70–74	16	14	1:0.8	5.9	3.1
75–79	6	1	1:0.1	2.2	0.2
80 or over	1	1	1:1.0	0.4	0.2
All ages*	268	449	1:1.6		
Total patients†	487	889	1:1.8		
Total relatives with diabetes	171	284	1:1.6		
Total diabetic patients and diabetic relatives	658	1173	1:1.7		

*Includes all cases with definite information as to date of onset of diabetes.

†Includes all cases and all ages with and without definite information as to date of onset of diabetes.

whereas among all patients the number of men was actually slightly greater than that of women. Considered by age of onset Jewish women patients in the late forties and fifties nearly twice outnumbered the men in both our and Joslin's series (Tables 4 and 5). In our group at the ages of sixty to sixty-four the ratio of men to women was even lower, namely 1:2.6. It increased, however, markedly at the ages sixty-five to sixty-nine. Joslin found that Jews constituted 11.6 per cent of his male patients, and Jewesses 16.3 per cent of all his female patients. The proportion of his Jewish patients to the total patients was maximum in the late thirties, namely 18.9 per cent for men and 24.2 per cent for women.

A study of our cases with a diabetic mate or with both parents diabetic shows the following results. We had 20 married couples with diabetes, from the ages of forty-eight to seventy-seven, mostly between sixty and seventy. Two couples had no children. Of the remaining 18, 6 of the couples each had 1 diabetic child.

Pannhorst[3] found that if two parents were afflicted with diabetes, or if one parent was so afflicted and the other possessed a familial predisposition toward the disease, 15 per cent of the descendants presented diabetes, whereas if the disease was present in but one parent only 1.5 per cent of the descendants were afflicted.

Among his Jewish patients Joslin[4] found that

TABLE 5. *Age at Onset, Sex Incidence and Ratio of Jews to All Diabetic Patients (Joslin et al.,[4] Boston, 1897–1928).*

Age at Onset	No. of Cases		Ratio of Men to Women	Per Cent of All Ages		Per Cent of Jews to All Cases	
	Men	Women		Men	Women	Men	Women
yr.							
Less than 20	20	40	1:2.0	5.5	7.5	—	—
20–24	15	11	1:0.7	4.2	2.1	12.0	14.3
25–29	18	17	1:0.9	5.0	3.2	11.0	12.7
30–34	32	32	1:1.0	8.9	6.1	15.6	22.5
35–39	48	53	1:1.1	13.3	10.0	18.9	24.2
40–44	59	70	1:1.3	16.2	13.3	18.3	22.3
45–49	54	101	1:1.8	14.9	19.0	13.6	21.8
50–54	56	101	1:1.8	15.4	19.0	12.4	19.9
55–59	32	61	1:1.9	8.9	11.6	9.5	13.9
60–64	19	26	1:1.3	5.3	4.9	7.0	8.7
65–69	6	13	1:2.1	1.7	2.5	5.1	7.0
70–74	2	2	1:1.0	0.6	0.4	2.9	2.9
75–79	—	1		—	0.2	—	3.0
Totals	361	528					
Averages			1:1.4			11.6	16.3

the onset picture was somewhat different from that of other patients. According to his experience (Table 5) the Jewish patients developed diabetes relatively early. The maximum numerical frequency of onset of diabetes in Jewish men was between the ages of forty and forty-four and in Jewish women between forty-five and fifty-four.

TABLE 6. *Age at Onset and Sex Incidence among Jewish Diabetic Patients (Combination of Tables 4 and 5).*

Age at Onset	No. of Cases		Ratio of Women to Men	Per Cent of All Ages	
	Men	Women		Men	Women
yr.					
Less than 20	31	49	1:1.6	4.9	5.0
20–24	19	16	1:0.8	3.0	2.6
25–29	22	22	1:1.0	3.5	2.2
30–34	42	51	1:1.2	6.5	5.2
35–39	73	80	1:1.1	11.6	8.2
40–44	89	123	1:1.3	14.1	12.5
45–49	85	177	1:2.0	13.5	18.1
50–54	100	181	1:1.8	16.0	18.5
55–59	75	131	1:1.7	11.9	13.4
60–64	46	96	1:2.0	7.3	9.8
65–69	22	32	1:1.4	3.5	3.2
70–74	18	16	1:0.9	2.8	1.6
75–79	6	2	1:0.3	0.9	0.2
80 or over	1	1	1:1.0	0.1	0.1
Totals	629	977			
Average ratio			1:1.5		
Grand totals*	1019	1701			
General ratio			1:1.6		

*Include our Jewish diabetic patients, their diabetic relatives and Joslin's Jewish diabetic patients.

Table 4 shows that the largest number of our Jewish men and women developed diabetes between fifty and fifty-four, the same age Joslin found for all his men and women patients. Root and Marble[5] from Joslin's clinic report in 1938 the maximum susceptibility to diabetes in all patients at the age of fifty-one for men and fifty-five for women. Further comparison of our table with Joslin's

shows a higher incidence of younger adults in his series of Jewish diabetic patients. This may be partially explained by the fact that all his patients are private and that younger people are more apt to go to a private clinic. Table 6 is compiled from Tables 4 and 5.

A study of the A and B blood groups and the

TABLE 7. *Frequency of A and B Blood Groups (Compiled in Part from Wiener[7]).*

	Author	No. of Persons	Incidence of Groups O %	A %	B %	AB %
Jews:						
Dutch	Herwerden	705	42.6	39.4	13.4	4.5
Polish	Holber and Mydlarski	818	33.1	41.5	17.4	8.0
Roumanian	Jonescu	1135	38.2	39.0	17.5	6.3
Macedonian	L. and H. Hirszfeld	500	38.8	33.0	23.2	5.0
Russian (Odessa)	Barinstein	1475	36.6	41.7	15.6	6.1
Jews (Boston)	Rudy and Keeler	444	36.7	40.7	16.4	6.0
Diabetic Jews (Boston)	Rudy and Keeler	200	43.5	32.5	16.5	7.5

M and N blood types has been carried out in some diabetic cases in order to determine whether there is any relation between the diabetic constitution and the known blood characters. In accordance with the suggestions of the Committee on Medicolegal Blood-Grouping Tests of the American Medical Association, the term "blood group" as used here refers to the blood groups O, A, B

TABLE 8. *Frequency of M and N Blood Types (Compiled in Part from Ride[8]).*

Author	Population	No. Investigated	Percentage Frequencies of Types M	N	MN
Landsteiner and Levine	New York City (whites)	532	26.1	20.3	53.6
Schiff	Berlin	1420	30.1	20.9	49.0
Thomsen and Clausen	Copenhagen	442	29.9	25.6	44.6
Wiener and Vaisberg	Brooklyn, New York	904	30.5	21.2	48.2
Hyman	Columbus, Ohio	578	30.1	22.0	47.9
Rudy and Keeler	Boston (diabetic Jews)	106	35.8	25.4	38.6

and AB, and the term "blood type" to the more recently discovered types M, N and MN.

Table 7 shows the frequency of the A and B groups in non-diabetic and diabetic Jews. The non-diabetic Jewish patients at the Beth Israel Hospital showed a blood-group distribution strikingly similar to that of Russian Jews. That of the Jewish diabetic patients showed no special characteristics.

M and N blood-type determinations were carried out on a group of diabetic patients and their relatives. Because of irregularities in the reaction of the M and N serums which we have obtained from time to time during our studies, we were forced to discard a large number of our tests, and the work was further limited by the fact that the serum is still difficult to obtain and is expensive. The data, therefore, cannot be considered sufficient to warrant any definite conclusions. It may be said, however, that the distribution of the blood types M and N in diabetic patients shows no striking difference from that in non-diabetic patients already reported in the literature (Table 8).

SUMMARY AND CONCLUSIONS

A study on heredity in Jewish diabetic patients has been carried out in over 1000 patients and compared with the findings of other authors, especially those of Joslin and his co-workers in Jewish and all diabetic patients. The results are as follows:

The family incidence of diabetes is four to six times as high in diabetic as in non-diabetic patients, and is higher in Jewish than in all diabetic patients.

Jewish diabetic patients at all ages show a higher incidence of the familial type of heredity than do all patients, and a higher incidence of the hereditary type at the younger ages.

Jewish female patients outnumbered men in a ratio of nearly 2:1.

The maximum susceptibility to diabetes in Jews (men and women) is at the age fifty to fifty-four, the same as in the population as a whole.

The distribution of the blood groups O, A, B and AB and of the blood types M and N in diabetic patients showed no striking difference from the distribution in non-diabetic patients.

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SURGERY OF THE EXTRAHEPATIC BILIARY TRACT*

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SURGERY of the biliary tract is almost never emergency surgery. Injuries to the liver or biliary tract, including the gall bladder, occur only with other intra-abdominal or thoracic trauma; this being so, they concern us only as part of the lesions present, and will therefore not be discussed here. Mechanical and inflammatory lesions bring nearly 100 per cent of the patients with gall-bladder, common duct and pancreatic disease to the surgeon, for less than 10 per cent have benign or malignant growths. Consideration must be devoted to those cases which most commonly require surgical treatment, and to the surgical procedures deemed most efficacious for their cure.

Acute and chronic inflammation of the gall bladder, obstructive conditions affecting the ducts, and new growths, both benign and malignant, are the pathologic conditions that most concern us.

Acute cholecystitis is a distinct surgical problem, and today, as when Murphy of Chicago, the Mayos, Ochsner and others were urging cholecystectomy as preferable to cholecystostomy or drainage, there is much discussion pro and con. But to me, an unanswerable argument against draining a gall bladder instead of removing it is the fact that I have seen 3 cases of primary carcinoma in gall bladders that had been drained. Every surgeon must have had similar experiences.

In the past year in our hospital there have been 2 cases of acute cholecystitis in which no surgical procedure was carried out, and in both cases the postmortem showed that operation had been indicated. This may seem a paradox when one remembers my first statement that gall-bladder surgery is never emergency surgery. But in one of these cases, seventeen days elapsed between the onset of the acute inflammation of the gall bladder and death from perforation and peritonitis. The other patient lived sixteen days after the onset of the disease.

Recently a patient on the medical service showed the initial signs of acute cholecystitis and was transferred to my service. After twice seeing her in consultation I considered that her attack was subsiding, as she had had a normal temperature for ten days, a decreasing leukocytosis and only moderate local tenderness. Yet at operation by my associate, on the nineteenth day of her disease, a large abscess was found outside the gall bladder. This parallels the finding in cases of acute appendicitis where the patient has survived the first two or three days of the disease, only to exhibit the signs of a hidden abscess.

An overweight patient past forty years of age, especially a woman with children, who has initial nausea and vomiting, usually with constipation and slight distention, and who has pain in the right upper abdominal quadrant, with local rigidity, some fever and moderate leukocytosis, presents a picture which should certainly indicate acute cholecystitis. There is no contraindication to this diagnosis because true gallstone colic does not occur, nor does any shoulder pain, and jaundice does not, except in the rare case, complicate the condition. Such patients should have surgical advice promptly, but it is advisable to postpone operation until the acute symptoms have subsided. In my opinion only the occasional case, because of gangrene of the organ, requires immediate operation, that is within the first forty-eight hours.

At operation, performed after due investigation and proper preparation, cholecystectomy should be carried out if possible. One often finds that a tense, plum-red gall bladder, which cannot be held or seized by any instrument, and the removal of which appears to be a hopeless task, will shell out easily after aspiration; and the postoperative course may be smoother than the days immediately preceding operation.

A résumé of my own cases shows that in 90 per cent the gall bladder was removed, and only 10 per cent were drained. Is abdominal drainage necessary? In almost all cases of cholecystectomy done for acute cholecystitis it is wise to insert a cigarette drain of soft-rubber dam, 2 cm. wide with gauze therein, down to Morrison's pouch, immediately underlying the sulcus of the gall bladder; this is removed gradually after four to six days. A surprising amount of serous exudate seeps into the dressings, and none into the peritoneal cavity. This prevents postoperative vomiting, hiccoughs and often even a serious local peritonitis. In a few cases the ligature on the cystic duct fails to hold and bile escapes. If this occurs while the drain or the sinus persists, no harm ensues, and the biliary fistula soon closes

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spontaneously. In one of our cases last year this biliary leak occurred after the sinus closed and we had a biliary ascites for weeks afterward. Aspiration was again and again necessary, and enormous amounts of bile, 3000 cc. at each aspiration, and later of bile-stained fluid, were removed. Eventually the upper third of the wound was reopened, the remaining fluid removed by suction, and a drain inserted, after which healing rapidly followed. This is the only case of free bile in the abdomen in large quantities that I have ever seen.

In chronic cholecystitis, with or without stones, the surgeon should be able to remove the gall bladder, reperitonealize the sulcus by suture, and close without drainage. This is the ideal operation, and these cases have less postoperative disturbance than occurs after simple appendectomy for acute appendicitis. Such patients usually have no vomiting, seldom even require an enema and are up and about in fourteen or sixteen days.

Where the common duct is opened in search for a stone or tumor, or to relieve stricture, the morbidity is greatly raised and the mortality is higher. The inexperienced surgeon, or the surgeon with adequate technical skill but not wide experience, is frequently at a loss to decide whether choledochotomy should be done. In a case of cholecystitis with gallstone colic where the gall bladder contains white bile, the common duct must be explored. White bile indicates obstruction, and this may be in the cystic duct. If so there will be no jaundice, the unit obtained by the van den Bergh test will not be raised. Jaundice which follows an attack of gallstone colic and is accompanied by a rising blood bilirubin, especially if irregular fever be present, with or without chills, points to a stone in the common duct which must be found and removed.

Patients who have been operated on and have had their gall bladders drained or removed not infrequently return with recurrent attacks of pain and jaundice and fever. If the common duct has not been opened at the primary operation, it is a fair assumption that they have a common-duct stone. If such symptoms follow soon after drainage of the common duct, inflammatory changes in the duct or cicatricial stricture is more likely.

Jaundice is only a symptom; it is not a disease. It is a sign of disease in the hematopoietic system, for example familial hemolytic jaundice; or of inflammatory obstruction in the liver bile channels, for example catarrhal jaundice; or of acute suppurative cholangitis and resulting pylephlebitis following a carbuncle on the neck. Again, jaundice may be the signal of obstruction in the ducts outside the liver, produced by calculi, by growths within the ducts, benign or carcinomatous, or by lymph nodes near the liver hilus; in two recent cases in our hospital such nodes were tuberculous, but they are usually malignant.

The surgeon must adapt himself to conditions diagnosed or to those found at operation. Therefore he should not open the abdomen to do an operation on the biliary tract, gall bladder or ducts unless he is competent to do any operation that may be required for the patient's relief. In cases where a gall bladder has to be drained, one may, in a week or two, easily find out if the biliary tract is free by the injection of 10 cc. of Lipiodol and olive oil into the biliary tree, after inserting a fine catheter into the sinus and using moderate pressure with a 20-cc. glass syringe. The hepatic duct and the common ducts are visualized by x-ray, and one may see the dye entering the duodenum. Any filling defect indicates stones or stricture and calls for further operation. In obstruction below the junction of the cystic and common ducts, anastomosis between the common duct or gall bladder and the duodenum or stomach will quickly result in the disappearance of the jaundice, a rapid fall in the blood bilirubin and, even in carcinoma, a quite long period of health and comfort for the patient.

Cholelithiasis is associated with so varied a symptomatology that it is as difficult to present all the facts as it is to count all the facets on all the stones found. In general it may be said that in the group of patients who have mild symptoms referable to the biliary tract, but in whom no stones can be demonstrated by x-ray, including dye studies, operation is not indicated. If, however, x-ray and the dye fail to visualize the gall bladder, and the patient has symptoms referable to it, operation is indicated although no stones are seen. If stones are proved to be present, even though they are associated with only mild symptoms, operation is indicated in order to prevent the complications of jaundice, acute cholecystitis, pancreatitis, and the like. William Mayo says that "innocent" or "silent" gallstones are a myth.

The onset of painless jaundice in a man of middle age or older is highly suggestive of carcinoma. A diagnosis of catarrhal jaundice is made at first, but must be reconsidered if the jaundice persists for a longer period than four weeks, and the van den Bergh test remains elevated. If pain initiates the attack of jaundice, then ceases, and the condition of the patient, even with the obstructive jaundice, is not progressively worse, a

stone in the common duct, often at the papilla of Vater, may well be diagnosed. Jaundice, even for so long a period as three years, has been cleared up rapidly in several cases by the removal of a so-called silent stone from the common duct.

The possibility of there being growths within the ducts themselves must always be borne in mind. I have found, as have my associates, both benign and malignant papillomas growing in the gall bladder and the common duct, and surgical removal of these growths is often possible. Intraductal carcinoma is, alas, too frequent a finding, and in the past two years there have been several cases on my service which worried us greatly. All these patients had painless jaundice, with the stool seldom clay-colored; indeed, the characteristic color was brown to a light sand color, varying from day to day and from week to week. The color index was always high, the jaundice never decreased and often the patient's well-being was remarkable. Two or three cases were operated on in an endeavor to relieve the jaundice, and if the gall bladder had not been removed at the first operation it was never ultimately found enlarged. Injection of the dye into the common duct at operation, and an x-ray plate taken on the operating table, would, I believe, at times make possible a diagnosis of the site of obstruction.

An unusual surgical condition which may confront the surgeon is exemplified in a recent private case of Dr. Archibald Stewart's, in which our assistant roentgenologist, Dr. J. W. McKay, diagnosed the condition from the x-ray findings when the patient was given a barium meal because of indefinite digestive symptoms. It was found that a large stone had ulcerated into the duodenum from the gall bladder: the barium regurgitated into the biliary system and was found even in the biliary radicles in the liver. Operation had to be carried out so as to prevent the ultimate formation of liver abscess.

Many cases with gallstones are easily diagnosed from the films taken following a barium meal. It is therefore our custom to take a flat plate of the abdomen in all cases where gastric symptoms are present, with or without signs pointing to the gall bladder, and, of course, in all cases where we suspect gallstones to be present. The dye, orally or intravenously, is used only after this simple procedure has been tried; and we never use dye in cases of jaundice, or where we believe there may be serious liver damage.

For the practitioner, the sound course is to consider that, potentially, surgical services are required by every case of gallstone colic, with or without jaundice, but with definite signs of acute inflammation in the right upper quadrant, namely pain, tenderness, muscle resistance and fever. And every case of jaundice initiated by severe pain, or, in middle-aged or elderly patients, coming on painlessly, should have a surgical consultation early. Till the medical attendant establishes a definite cause and is sure there is nothing more than a simple catarrhal jaundice present, his responsibility is as great as in the early hours of acute appendicitis. As in the cases of gastric and duodenal ulcer, medical treatment should be the first treatment, often the sole treatment, but at times, surgical treatment becomes the only procedure that is justified. In ulcer, long duration of symptoms, hemorrhage, gastric retention or perforation indicates the necessity for surgery. So, too, cholecystitis, stones and jaundice, secondary disturbances of sugar metabolism and pancreatitis call for surgery, sometimes as in ulcer, promptly and urgently. Usually, however, due consideration may be given to the time, the place and the surgeon.

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COMPLETE HEART BLOCK RESULTING FROM OVERDOSAGE WITH THYROID EXTRACT*

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THE purpose of this paper is to report a case of complete heart block resulting from excessive dosage with thyroid extract. So far as we have been able to ascertain from a review of the literature, there has never been a similar case recorded. Although this case represents an instance of induced hyperthyroidism, nevertheless certain correlations with true hyperthyroidism may be made.

The effects of uncomplicated hyperthyroidism on the cardiovascular system are well known. Dyspnea on exertion, palpitation, tachycardia, elevated blood pressure with increased pulse pressure, decreased vital capacity, diffuse and forceful apex beat, snapping heart sounds and apical and basal systolic murmurs are met with to a certain extent in almost all thyrotoxic patients. Disturbances in auricular contractility, among which may be mentioned auricular fibrillation, either permanent or paroxysmal, auricular flutter, auricular premature beats and paroxysmal auricular tachycardia are not infrequently encountered. Of rare occurrence is the presence of defective auriculoventricular conduction. The incidence of partial heart block in hyperthyroidism has been studied by a number of investigators, and varied results have been reported. Willius, Boothby and Wilson[1] in 1923 reported 1 case in a series of 298 which showed a prolonged P-R interval. Dameshek[2] in 1924 reviewed 141 cases, 2 of which had partial heart block. A greater incidence of delayed auriculoventricular conduction resulted from a study of 787 cases by Goodall and Rogers[3] a few years later, in which a prolonged P-R interval was found in 242 cases. In 225 cases of hyperthyroidism at the Boston City Hospital we were able to find only one case with a P-R interval above the normal. A more detailed review of the literature has been given by Davis and Smith.[4] There is general agreement, however, concerning the great rarity of complete auriculoventricular dissociation in cases of hyperthyroidism. The first recorded case was that of Merklen in 1882.[5] Since that time there have been reported 1 case by de Vries Reilingh[5] in 1915, 2 cases by Dameshek[2] in 1924 and 6 cases by Davis and Smith[4] in 1933, a total of 10 cases. There are no reports of cases in which the condition was induced by the administration of thyroid extract.

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CASE REPORT

A 33-year-old white, married Jewess was admitted to the First Medical Service of the Boston City Hospital on May 23, 1938, complaining of diarrhea of 1 week's duration and vomiting of 2 days' duration. The diarrhea continued unabated to the time of entry, and consisted of frequent watery stools containing no mucus, blood or pus. Vomiting occurred 5 days after the onset of the diarrhea and followed immediately the ingestion of any food by mouth, either solid or liquid. There was no abdominal pain, and other constitutional symptoms were lacking. A diagnosis of ptomaine poisoning was made by a local physician, and hospitalization was advised. One month prior to admission the patient was treated at home for a septic throat and enlargement of the cervical lymph nodes. Recovery was complete at the end of 2 weeks.

Three years before admission the patient was advised to take thyroid extract because of obesity associated with a low basal metabolic rate. Supervision of the dosage of the thyroid extract, however, was not sought, the patient having promptly resorted to the medication whenever she noticed an increase in weight. An accurate estimate of the amount of the drug taken during this period could not be obtained. For 5 weeks prior to the onset of the present illness she had been taking four or five 2-gr. tablets of desiccated thyroid extract (Parke–Davis) daily, which was 50 per cent stronger than the U.S.P. thyroid extract. She was thus taking the equivalent of from 12 to 15 gr. of the extract daily. The remainder of the past history was non-contributory.

Physical examination showed a well-developed and well-nourished woman, apprehensive, restless, tossing about in bed, retching frequently and begging for water, which she would immediately vomit after taking a few sips. She was very nervous and irritable and at times became hysterical. The skin was sallow in appearance, dry, warm and inelastic. The tongue was coated and quite dry, and the mucous membranes of the mouth in general showed evidence of dehydration. There was a fine tremor of the extended tongue and the extended fingers. The eyes, ears and nose were negative. The external jugular veins were moderately distended. There were no masses, bruits or abnormal pulsations in the neck. The chest was symmetrical and of equal expansion, and the lungs were clear and resonant throughout. The heart was not enlarged; the sounds were of good quality, regular and slow, the rate being 32; P_2 was greater than A_2; no murmurs were heard. The abdomen was negative. The extremities were not remarkable. It was difficult to elicit the deep reflexes. The blood pressure was 110/64. The temperature was 97.8°F., the pulse 32, and the respirations 20.

The urine on admission showed a specific gravity of 1.010, a slight trace of albumin, no sugar and a sediment containing rare red and white cells. The hemoglobin

(Sahli) was 70 per cent, the red-cell count 3,630,000 and the white-cell count 25,600. A blood smear showed 88 per cent polymorphonuclears, 6 per cent lymphocytes, 5 per cent monocytes and 1 per cent myelocytes; the red-blood cells and platelets appeared normal. The nonprotein nitrogen was 83 mg., the plasma chlorides 504 mg. per 100 cc., the carbon-dioxide combining power 22.0 vol. per cent and the cholesterol 234 mg. per 100 cc. A blood Hinton test was negative. Stool examinations were negative.

An attempt was made on admission to check the diarrhea, which was quite troublesome, by the oral administration of paregoric and bismuth subcarbonate. Vomiting continued and parenteral fluids containing glucose, saline and iodine were resorted to. On the following day the vomiting was somewhat less. The pulse was still slow, averaging 30, and there were short periods of apnea associated with convulsive seizures, epileptiform in type, lasting from 10 to 15 seconds. An electrocardiogram showed the following: auricular rate 94; ventricular rate 26 to 33; QRS complex 0.08 to 0.12 second; T_1 upright, T_2 upright with low origin, T_3 upright, T_4 upright with low origin; left ventricular predominance; ventricular premature beat in Lead 4; changing ventricular pacemaker. The interpretation was "complete heart block, myocardial disease." During the next 36 hours the patient remained anuric, but responded finally to several intravenous injections of hypertonic saline. Signs of bronchopneumonia were elicited at the left base. The pulse rate was then 88, and the rhythm regular. A repeat electrocardiogram showed normal sinus rhythm, auricular and ventricular rates 88; P-R interval 0.20 second; QRS complex 0.08 second; T_1 low, T_2, T_3 and T_4 upright; axis normal. The interpretation was "within normal limits." Throughout this period the patient appeared quite drowsy and apathetic and responded only sluggishly to stimulation. By the 5th hospital day the nonprotein nitrogen had reached 150 mg. per 100 cc., and the creatine 6.2 mg. The blood chlorides were 595 mg. per 100 cc., and the carbon-dioxide combining power 26 vol. per cent. A portable chest plate showed areas of pneumonitis at the left cardiophrenic angle. Parenteral fluids containing saline, glucose and sodium bicarbonate were continued. Three days later there appeared slight pitting edema about the ankles and the parenteral administration of fluids was stopped. The urinary output gradually but steadily increased and the nonprotein nitrogen slowly fell; on the 8th hospital day it was 120 mg. per 100 cc. The signs at the left base were clearing, the sallow appearance of the skin was no longer present and the general condition of the patient was markedly improved. During the subsequent week the nonprotein nitrogen rapidly fell to 37 mg. per 100 cc. Physical examination at that time was essentially negative. On the 23rd hospital day the patient was allowed up, and 10 days later she was discharged. At the time of discharge the basal metabolic rate was —18 per cent, the blood cholesterol was 147 mg. per 100 cc., and the electrocardiogram was normal.

COMMENT

A review of the literature reveals many conditions which have been associated with complete heart block. Among the infectious processes may be mentioned tonsillitis, rheumatic fever, diphtheria, pneumonia, gonococcal and other septicemias, influenza and subacute bacterial endocarditis. In these cases the block has been ascribed to the presence of localized inflammation in the A-V bundle or in areas adjacent to it. Occasional reports of complete heart block accompanying uremia have been noted. With respect to the case here presented, both pneumonic and uremic manifestations existed. However, it should be noted that evidences of pneumonia did not develop until four days after admission, at which time the heart rate and rhythm were normal; also that the blood nonprotein nitrogen did not reach its maximum until the fifth hospital day, two days after the heart had returned to normal. We feel, therefore, that the presence of complete heart block in our case is to be attributed to the toxic state induced by the excessive doses of thyroid extract and to other less well-defined factors to be considered later.

Concerning the pathogenesis of complete heart block in thyrotoxicosis much remains to be learned. In an attempt to explain the block on the basis of anatomic lesions certain difficulties are encountered. There is, first of all, little evidence available at the present time in support of this concept. In a review of the literature pertaining to the pathologic changes in the myocardium incident to hyperthyroidism, there is found a great difference of opinion not only as to the nature of the morphological lesions but also as to whether such lesions actually exist. On the basis of both experimental and clinical studies several authors report varied changes in the heart muscle, among them being myocardial necrosis, cellular invasion, fatty vacuole formation, moderate fibrosis, fraying of muscle bundles and alterations in the staining properties of the muscle fibers. On the other hand, some investigators deny that such lesions are specific and others that they exist at all. The theory that the hearts of patients with hyperthyroidism are more susceptible to injury by infection and other toxic agents than those of normal persons was put forth many years ago. Goodpasture[6] in 1921 called attention to this fact. In the more recent report of Davis and Smith[4] the role of infection is greatly stressed. However, in a careful study of these cases it appeared to us that there was a great discrepancy between the time relation of the infection (usually tonsillitis) and the appearance of the complete heart block. The presence of fever and toxic agents liberated during stormy postoperative courses could not be ruled out as agents contributing to the block. At necropsy of a fatal case these authors noted an inflammatory lesion involving the bundle of His, in which could be demonstrated infiltration by polymorphonuclear leukocytes and monocytes, edema, and questionable gram-positive bacteria, either diplococci or short-chain streptococci. The

exact pathogenesis of this lesion, however, is not clear. In a report of a single case by Steuer[7] the heart block seemed to be a function solely of the hyperthyroidism.

In analyzing the numerous accounts of the pathological studies, certain deductions may be made. There seems to be sufficient evidence to warrant the conclusion that hyperthyroidism increases the susceptibility of the myocardium to injury by toxic agents. In some cases definite and varied anatomic changes do occur in the myocardium. It is quite conceivable that the development of these lesions somewhere along the bundle of His may explain the occurrence of complete heart block. This is apparently well illustrated in the fatal case of Davis and Smith. It is true that such lesions are rare. It is likewise true that complete heart block during the course of hyperthyroidism is also rare.

An aspect of this problem which has been somewhat neglected is the physiological one. As a result of the prolonged overactivity of the heart and the changes in the metabolism of the cells induced by the thyrotoxic state, the nutritional stores of the myocardium may become greatly exhausted. It has been repeatedly demonstrated that in experimentally produced hyperthyroidism the cardiac muscle is found to be free of glycogen, both by microscopic examination and chemical analysis. It is well known that cells from which the glycogen has been removed are rendered more susceptible to infection and other toxic agents. Morphologic changes in the myocardium may result, these being secondary to the altered state of nutrition rather than to any specific action by the thyroid secretions. Further evidence of deranged nutrition of the myocardium is afforded by the work of Bodansky,[8] who demonstrated that in rats the administration of thyroid extract and thyroxine reduced the creatine content of the heart muscle to 50 per cent of normal. A more striking depletion of phosphocreatine was observed in a smaller series of experiments. In a later communication Bodansky and Pilcher[9] noted that the restoration of the creatine concentration of the myocardium to normal occurred quite rapidly, and was well in advance of evidences of tissue repair. In some cases normal values for creatine were found in the presence of moderate myocardial damage. That similar changes occur in the phosphocreatine concentration of the Purkinje system is quite probable. It would seem not unlikely, then, that the transient and, in certain cases, paroxysmal nature of some of the cardiac arrhythmias observed during the course of hyperthyroidism is a function not of morphologic changes in the myocardium but rather of chemical alterations, many of which are readily reversible. In the case reported here, the transient nature of the heart block is apparent.

In accounting for the cardiac manifestations of hyperthyroidism, then, many factors must be taken into consideration. The altered metabolism and state of nutrition of the myocardium, together with other altered physiologic processes, the depletion of glycogen from the cardiac muscle, the reduction in the concentrations of creatine and phosphocreatine, the resultant susceptibility of such muscle to toxic and infectious agents, the morphologic alterations consequent to such nutritional disturbances and finally the possibility of a specific toxic agent elaborated by the thyroid gland and producing specific lesions by itself must be evaluated. The evidence for the last, at the present time, is quite meager. To attribute the presence of heart block to any one of the other abovementioned factors is, considering the state of our knowledge, still unjustified. The answer to the problem will more likely come from a consideration of a combination of these factors, and after more careful physiological and pathological study of both experimental and clinical material has been made.

SUMMARY AND CONCLUSIONS

A case of complete heart block resulting from overdosage with thyroid extract is reported. A review of the literature since 1882 reveals a total of 10 cases of complete heart block developing during the course of true hyperthyroidism, but no cases in which the block was induced by the administration of thyroid extract.

A brief discussion of the factors involved in the pathogenesis of complete heart block in hyperthyroidism is attempted. The transient nature of the heart block in the reported case suggests that the disturbance may be a function of reversible chemical changes in the myocardium rather than of morphologic alterations.

The case represents an excellent illustration of what may be expected from the uncontrolled use of thyroid extract in the treatment of obesity.

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REPORT ON MEDICAL PROGRESS

BACTERIOLOGY*

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BACTERIOLOGY has made considerable progress in recent years, largely because of the increasing application of the methods of physics and chemistry to its problems, the development of antigen analysis and the growing importance of the virus diseases. For the busy practitioner who wishes to keep abreast of this advance, a few publications can be especially recommended. In the journals, the annual review by Reimann[1] published in the *Archives of Internal Medicine* covers the field of clinical infectious disease, while some of the monographs appearing in *Bacteriological Reviews* summarize important laboratory investigations in special fields. Two new books should prove particularly valuable, one on sulfanilamide by Long and Bliss,[2] the other on immunology and its practical application to medicine, surgery and public health by Zinsser, Enders and Fothergill.[3]

In this report we shall attempt to survey the recent advances in bacteriology in a broad way and select a few topics for detailed analysis which have a bearing on clinical practice.

BACTERIA

The main interest in bacterial infections is focused on chemotherapy, which we shall discuss below. In pure bacteriology recent studies have been concentrated on the metabolism and chemical structure of bacteria. Much has been learned about the exact conditions governing bacterial growth, the enzyme systems whereby micro-organisms obtain their energy[4] and the nutritional requirements of individual bacterial species.[5] The last-named investigations have led[6] to the development of synthetic media of known and reproducible composition, which have been particularly useful in the production and purification of diphtheria toxin.

Following the isolation of bacterial "residue antigens" by Zinsser and Parker[7] and their definition as carbohydrates by Heidelberger and Avery,[8] the pathogenic micro-organisms have been subjected to an extensive immunological and chemical analysis, which has progressed farthest with the pneumococcus. As originally isolated, the specific soluble substance or type-specific carbohydrate of the pneumococcus was considered to be a haptene (capable of reacting with specific antiserums but incapable of inducing antibody formation), but it has now been shown to represent a chemically altered product of the substance as it exists in the living organism. By methods of extraction which maintained an acid reaction throughout, Enders,[9] as well as Avery and Goebel,[10] isolated the mother substance, an acetylpolysaccharide which possesses antigenic properties of its own. Similar active fractions have been isolated from hemolytic streptococci[11] and the brucella,[12] typhoid[13] and salmonella[14] organisms. Immunization of human beings with these chemically purified antigens is still in the experimental stage, but Felton[15] has attempted it for pneumonia. It is conceivable that our present vaccines may in time be supplanted by these preparations, since the latter possess greater stability, uniformity and potency. This work has been carried to its logical conclusion by Goebel[16] with the synthesis of an artificial antigen, obtained by coupling cellobiuronic acid, on which the type specificity of the Type 3 pneumococcus polysaccharide depends, to a protein by the diazo reaction. Serums from rabbits immunized with this compound gave strictly type specific agglutination and *Quellung* reactions but conferred protection on mice against Types 2 and 8 as well as Type 3.

Such work was made possible by Landsteiner's[17] fundamental studies on the nature of antigens, which have shown that despite their large molecular size the immunologic specificity depends on the presence of simple chemical groups or even stereochemical arrangements. This supports Ehrlich's original hypothesis of the chemical nature of antigen-antibody union, whereas studies on the nature of antibodies have shown that many features of Bordet's theory of the colloidal nature of immunologic phenomena are also true, since antibodies are large protein molecules which behave as colloids. It has been possible to obtain purified antibody solutions and thus to study the size, physical properties and chemical behavior of antibody molecules. In quantitative studies with chemically pure reagents, Heidelberger and his coworkers[18] have shown that the union of antigen and antibody is a reversible one in accordance with the laws of mass action, as originally postulated by Arrhenius.[19] Since the union of anti-

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gen and antibody can take place in multiple proportions rather than in single-formula masses, the neutralization of diphtheria toxin by antitoxin occurs along a wide zone instead of at a single point.[20] It is not possible, therefore, to postulate a single mass-action law for these reactions. Goodner, Horsfall and Bauer[21] have shown that antibody size varies with dilution, so that, for example, a given amount of antipneumococcus serum will combine with much more specific polysaccharide when it is diluted than would be expected from its original concentration. This may help to explain the observation of Nye and Harris[22] that the amount of antipneumococcus serum necessary to neutralize the specific soluble substance present in a consolidated lung was many times the effective therapeutic dose.

Chemotherapy

The introduction of sulfanilamide has made it possible to treat a large number of bacterial infections successfully, but has placed a greater responsibility on the clinician. He must make a rapid bacteriological diagnosis, be alert for toxic symptoms which often simulate those of the disease itself, and learn to judge the status of an infection which has been artificially modified by treatment. Since the practical aspects of sulfanilamide therapy have been covered in other progress reports in this series, we shall attempt to review what is known of its mode of action in hemolytic streptococcal infections. We believe that the use of related compounds such as sulfapyridine and the chemotherapy of other types of infection should be governed by the same principles.

Sulfanilamide owes its remarkable curative properties both to its efficacy against the infecting organism and to its rapid absorption, ready diffusibility into the tissues and lack of toxicity at therapeutic concentrations.[23] These pharmacologic properties are lacking in many other chemotherapeutic agents previously developed, which are much more potent in vitro. In fact, sulfanilamide interferes so delicately with the balance between the infecting organisms and the defensive reactions of the host that there has been doubt about which of these two components it affects. However, there is little evidence[24] that the drug stimulates the defense reaction and abundant evidence[25, 26] that it makes the organism less virulent and thus amenable to destruction by the natural processes of resistance. How it does so remains somewhat of a mystery, but certainly it slows down the rate of multiplication of the bacteria.[27, 28] This bacteriostatic effect, which has been clearly demonstrated in animals by Rambo,[29] varies in the test tube with different environmental conditions. In general, the more favorable the environment for the streptococci the less effective sulfanilamide becomes. The accompanying table, modified from one in the recent article of Gay et al[30] is self-explanatory.

Factors Influencing the Effect of Sulfanilamide on Hemolytic Streptococci.

Variables	Factors Favoring the Organisms	Factors Enhancing the Effectiveness of Sulfanilamide
Medium in which organisms are growing	Tissue debris — peptone[31] Diminished oxygen tension[32, 33]	Pure serum or blood[31] Elevated oxygen tension[32, 33]
Temperature	Normal body temperature	Fever (sulfanilamide bactericidal above 39.5°C. in vitro[34]) Tillett phenomenon[35] (serum of febrile patients develops bactericidal power against hemolytic streptococci)
Bacteria	Strain resistant to sulfanilamide Large numbers[27] Highly virulent strain	Strain susceptible to sulfanilamide Small numbers[27] Avirulent strain*
Phagocytes	Leukopenia	Leukocytosis
Immunity	No antibodies	Antibodies
Blood sulfanilamide	Low or fluctuating level	Constant effective level (7–15 mg. %)

*Some observations[24] tend to show that sulfanilamide is less effective against avirulent than against virulent strains in vitro, but infection with virulent organisms is naturally more difficult to control.

Most of the factors favoring sulfanilamide operate in the blood stream and sites of rapid invasion, where the organisms are growing in tissue fluid containing serum. Those favoring the organisms are found in the areas of local infection, where large numbers of bacteria are growing at a diminished oxygen tension in a medium enriched by the products of tissue breakdown. In clinical and experimental infections the blood stream may be cleared fairly soon after treatment is begun, but the local infection persists much longer, and if sulfanilamide is discontinued too soon, the whole process will recur. Although it may be bactericidal under the most favorable circumstances,[31, 36] sulfanilamide usually acts only as a bacteriostatic agent, so that phagocytosis is essential in order to get rid of the infecting micro-organisms. Since specific antibody is necessary for the phagocytosis of fully virulent organisms,[37] the degree of immunity of the host is very important. The administration of specific anti-serum has been shown to enhance the effectiveness of the drug in laboratory experiments.[38] This has been amply confirmed in the clinic by Finland et al.,[39] using serum and sulfapyridine for severe pneumococcal infections, and by Lyons and Mangiarcine,[40] with immunotransfusion and sulfanilamide for hemolytic streptococcal septicemia. Although it has been suggested that sulfanilamide suppresses antibody formation,[41] the evidence indicates that this only happens when the infection is treated so early that an insufficient antigenic stimulus occurs. This is an added reason for continuing treatment for several days after an apparent cure, since

relapses will be more dangerous and more frequent if immunity has not developed.

On the basis of existing knowledge, sulfanilamide is indicated in practice in all severe infections due to the hemolytic streptococcus, meningococcus and gonococcus and in infections of the urinary tract. Cases of gas gangrene, brucellosis (undulant fever) and influenza bacillus meningitis also should receive sulfanilamide, although the evidence for its efficacy is still incomplete. Since sulfapyridine is irregularly absorbed and produces nausea and vomiting in most patients, its use should be restricted to pneumococcal infections and desperate diseases such as bacterial endocarditis and staphylococcal sepsis, where its greater potency may be decisive. It should be emphasized that these drugs are not panaceas and do not supplant all well-established medical and surgical therapy. They are more effective as prophylactic than as therapeutic agents, and we believe moderate doses should be given to cases of severe crushing injury, as prophylaxis against gas gangrene, or perforation of a viscus, where peritonitis may be expected. During treatment an adequate concentration of the drug must be constantly maintained in the body fluids, for if it is allowed to fall below the effective level the organisms again begin to grow rapidly. Therefore oral administration and frequent dosage are recommended.

The development of an entirely new approach to chemotherapy is due to the efforts of Dubos and Avery. In 1932 they[42] discovered, in a bacillus isolated from a peat bog, an enzyme capable of hydrolyzing the capsular polysaccharide of the Type 3 pneumococcus. Preparations of this enzyme cured infected animals by destroying the capsules of the organisms, thus making their phagocytosis possible.[43] Since then Dubos has been searching for a similar substance which would attack bacterial bodies. He reasoned that, since the decomposition of organic matter in soil was effected by micro-organisms, he might be able to develop a strain of soil bacteria capable of decomposing bacterial protein. He kept adding washed cultures of gram-positive cocci to a sample of soil and eventually isolated a gram-positive bacillus, culture filtrates of which were bactericidal for all the gram-positive but for none of the gram-negative species tested. He[44] has now obtained the active principle in nitrogen-free form, so potent that a small fraction of a milligram will kill cultures in vitro and protect mice against many fatal doses of pneumococci and streptococci.

Active Immunization with Toxoids

In 1925 Ramon[45] showed that if diphtheria toxin was incubated with formalin for a long time it gradually lost its toxicity but retained its antigenic properties. Such altered toxin, called toxoid or anatoxin, is superior to toxin-antitoxin as an immunizing agent, but contains considerable diphtheria bacillus protein, to which many people become sensitive during life, so it can be given only to children under five or six years of age. For this reason, the purification of diphtheria toxin by Eaton[46] and by Pappenheimer[47] is very important, and it should soon be possible to obtain pure toxoid, safe for use at all ages. Toxoid may be used as such or in the alum-precipitated form recommended by Glenny et al.[48] With the latter, fewer injections are given at longer intervals, since the antigen is fixed at the site of injection, from which it is very slowly liberated.

Toxoid may also be prepared from tetanus toxin by similar methods[49] and has recently been used for human immunization.[50] Since sensitivity to tetanus bacillus protein does not normally develop, it can be used at all ages without danger of severe reactions. It confers an active immunity, which rises slowly, reaching its peak after several months. The duration of the immunity is uncertain but probably extends for several years. Within a year or two after the primary course of immunization, a single injection (*injection de rappel*) produces a renewed and more rapid rise in the titer of antitoxin, which reaches its peak in two or three weeks and then slowly falls over many months.[51] Such a procedure has advantages over the prophylactic injection of tetanus antitoxin, since the latter does not raise the titer to so high a level, lasts only two weeks and sensitizes the patient to horse serum. This is important in connection with the possible necessity for repeated injection of antitoxin at the time of repair operations weeks after the injury. The one drawback to the practical application of tetanus toxoid is the lack of a test analogous to the Schick test for determining whether immunization has succeeded. However, active immunization against tetanus is indicated for soldiers and people in hazardous occupations, and in civilian life is justified by its protection against the many minor injuries which are too trivial to require the use of antitoxin, but which are always a source of worry to the physician. Since these are particularly common in childhood many pediatricians are giving combined tetanus and diphtheria toxoids at the time of routine immunization against diphtheria. Dosage consists of three 1-cc. doses of plain toxoid at intervals of two or three weeks, or two 1-cc. doses of alum toxoid at intervals of two months. At present, if a previously immunized patient is severely injured, he should probably receive not only a single injection of

toxoid but the usual dose of antitoxin for immediate protection. Experience in the future may show that the latter is unnecessary.

Staphylococcus toxoid has been recommended for the treatment and prevention of chronic staphylococcal infections, particularly boils. Since the immunology of these infections is poorly understood we shall not comment on this recommendation. Satisfactory scarlet fever toxoid has not been prepared.

FILTERABLE VIRUSES

Perhaps the most rapid advances have been made in this field. A virus etiology has been proved for a number of important diseases: trachoma,[52] lymphogranuloma inguinale,[53] yellow fever,[54] influenza[55] and canine distemper.[56] Measles is probably a virus disease, but although it has almost certainly been transmitted to monkeys by Blake and Trask,[57] absolute proof of its etiology is still lacking. The isolation of influenza virus was the result of Laidlaw's discovery that canine distemper was transmissible to ferrets. Influenza has now been transmitted through ferrets to mice,[58] and thus a great deal of experimental work has been possible that could not have been done with larger animals. Although human influenza is a pure virus disease, it is interesting that swine influenza, in its typical form, is due to two agents, a filterable virus closely related to the human virus and the swine influenza bacillus.[59] This fact has aroused much speculation concerning the role of a virus in paving the way for bacterial invasion of the respiratory tract. This hypothesis has been proved wrong for pertussis,[60] but Dochez et al.[61] claim to have isolated a "cold" virus which causes human coryza and paves the way for pneumonia. The latter theory must be confirmed. Among the many new virus diseases described in recent years, the most important are those of equine encephalomyelitis[62] and benign lymphocytic choriomeningitis.[63]

The sizes of various viruses have been measured by ultracentrifugation and ultrafiltration, and it has been found that they cover a very wide range. The largest viruses, such as that of vaccinia, overlap the smallest bacteria and have infective units which are microscopically visible as elementary bodies, from which different antigenic fractions can even be extracted. The smallest viruses approach the size of the largest known molecules, the proteins. The virus of tobacco mosaic disease has been obtained by Stanley[64] in what he believes to be a pure crystalline form, and is a nucleoprotein with a probable molecular weight about twelve times that of horse globulin.

As studies of immunity in virus diseases progress, its essential similarity to antibacterial immunity becomes increasingly apparent.[65] Whatever differences there are depend on the different spheres of activity of the two types of pathogenic agents, since bacteria multiply in the tissue spaces, while viruses can only multiply inside living cells. Most of the difficulties of virus work spring from this obligate intracellular parasitism.

Successful cultivation of the viruses can be carried out only by growing them in living susceptible cells, and the virus so obtained is really a mixture of virus and tissue proteins. Many viruses can be readily adapted to tissue culture or laboratory animals, but others, such as that of poliomyelitis, cannot be. Immunological studies must make use of the animal protection test, except in the case of a few virus diseases where special serologic reactions have been devised, such as the flocculation test in vaccinia.

Neutralizing antibodies, analogous to antibacterial antibodies, develop after most virus diseases, and their presence has been widely used by epidemiologists as proof that the patient has had a specific infection. In a study of yellow fever, its world distribution has been mapped by determination of mouse protective antibodies in representative samples of human serums.[66] Similar epidemiological studies of influenza are in progress, but the work is complicated by the number of immunologically distinct strains of the virus.[67]

Until recently it was thought that active immunization against any virus infection required the injection of living virus. Satisfactory vaccination against yellow fever has been achieved by attenuation of the virus by repeated passage through mouse brain and chick embryo for several years, and by injecting this living attenuated virus subcutaneously.[68] But we now know that active immunization against certain viruses is possible with killed vaccine if enough can be injected.[69] Thus, any methods of virus cultivation which yield higher titers of virus in tissue are of great importance. Goodpasture and his colleagues have shown that the developing egg makes an ideal culture medium for many viruses.[70, 71] For instance, the virus of equine encephalomyelitis reaches a very high concentration in the embryo, and this embryonic tissue, ground, filtered and formalinized, makes a potent vaccine.[69] Zinsser and his associates[72] have been able to cultivate large amounts of tissue on the surface of agar slants and thus obtain large yields of rickettsiae for the making of typhus vaccine.

The therapy of virus infections has made little progress. Chemotherapy has proved of little value[73] except in a few cases where its action is probably on secondary bacterial invaders.[74] Convalescent serum has failed to influence the course

of these diseases, although it has been extensively tried in poliomyelitis,[75] but recent work with measles suggests that if convalescent serum is given early and in large amounts it may modify the disease.[76]

RELATION OF ANIMALS AND INSECTS TO HUMAN DISEASE

Although the transmission of disease from animals and insects to man is not a new concept, a number of recent discoveries have shown that more types of disease are spread this way in New England than has been generally recognized. Tularemia is the most important bacterial infection in the United States which is so transmitted. First recognized and described by members of the United States Public Health Service and now being found in many parts of the world, it is a naturally occurring disease of wild rodents, among which it is transmitted by the bites of bloodsucking insects.[77] The common tick of this region, the dog tick, *Dermacentor variabilis,* may harbor the infection, but in the wood tick, *Dermacentor andersoni* (fortunately a Western species), the bacterium, *Pasteurella tularensis,* is handed down from generation to generation in the ovum. Human cases develop from handling infected ticks or animals (mainly rabbits, although a great many animals are susceptible) or from the bites of infected flies. The recent case on Cape Cod[78] and the prevalence of ticks and rabbits suggest that this disease may become more frequent in this area.

Rickettsial infections are now recognized in all parts of the world.[79] Rickettsiae are tiny intracellular parasites of insects which are capable of infecting certain animals, including man. Although typhus may always appear, Rocky Mountain spotted fever is the important member of this group for New England. This disease, which occurs every summer in Virginia, Maryland and Pennsylvania, has recently been diagnosed in Rhode Island and southern Massachusetts.[80] The infection, like tularemia, is hereditarily transmitted in ticks and is contracted from contact with an infected tick. The disease is characterized by a high fever lasting about two weeks, a maculopapular or petechial rash, particularly on the extremities, and stupor and irritability. Diagnosis is made by the development of a positive Weil-Felix reaction (agglutination of *Bacillus proteus* X 19) about ten days after onset or by the production of characteristic fever in a guinea pig after the intraperitoneal injection of 5 cc. of blood taken during the first week of the disease. As yet the disease is not common enough to justify any prophylactic measures except a healthy respect for ticks, although a vaccine of formalinized rickettsiae can be prepared. Sulfanilamide is useless in treatment.[81]

Equine encephalomyelitis is a severe epidemic disease of horses caused by a virus, of which a number of immunologically distinct strains have been described. The disease attracted widespread attention last summer, because an epidemic among horses in southern Massachusetts[82] due to the Eastern strain of the virus was accompanied by a number of proved human cases,[83] characterized by a high mortality and severe sequelae. Human encephalitis due to the Western strain of the virus was also recognized last year.[84] Following the work of Kelser,[85] who transmitted the virus from horse to horse by the bites of *Aedes aegypti* mosquitoes, it was assumed that the disease spread among horses in this way. But the discovery of the virus in pigeons[86] and wild pheasants[87] has suggested that it may have its reservoir in wild birds, from which it is transmitted to horses and perhaps to man. Field proof of its transmission by the mosquito is lacking for this cycle.

Equine encephalomyelitis has provided the laboratory with an ideal virus for investigative work. It is pathogenic for a great number of small animals, and in the embryo chick the virus reaches a very high titer. This has enabled Beard, Finkelstein, Sealy and Wyckoff to produce a potent vaccine,[69] and they have already been able to obtain the virus in a comparatively pure state by differential centrifugation of the ground chick-embryo tissue.[88] This vaccine, produced primarily for the immunization of horses, is applicable to human beings, but unless the disease becomes much more prevalent than its past history would suggest there should be no call for its general use.

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NEW HAMPSHIRE MEDICAL SOCIETY

PROCEEDINGS OF THE ONE HUNDRED AND FORTY-EIGHTH ANNIVERSARY

House of Delegates, June 8 and 9, 1939

The House of Delegates convened at the Hotel Carpenter, Manchester, on Thursday morning, June 8, 1939, at 8:30, with Speaker W. J. Paul Dye, of Wolfeboro, presiding.

The following members answered the roll call:

The President, ex-officio
The Secretary-Treasurer, ex-officio
Chester L. Smart, Laconia
Francis J. C. Dube, Center Ossipee
Osmon H. Hubbard, Keene
Leslie K. Sycamore, Hanover
John C. Eckels, Lisbon
Willard A. Bates, Littleton
Deering G. Smith, Nashua
George C. Wilkins, Manchester
Emery M. Fitch, Claremont
Clarence E. Dunbar, Manchester
George V. Fiske, Manchester
Henry O. Smith, Hudson
Fred Fernald, Nottingham
Wendell P. Clare, Portsmouth
Norman K. Chesley, Rochester
Henry C. Sanders, Jr., Claremont

SPEAKER DYE: The first order of business this morning is the report of the Committee on Communications and Memorials.

DR. DUBE: We have a telegram from the Coos County Fiscal Agent, asking the New Hampshire Medical Society to co-operate by appointing a committee to study Coos County medical relief costs.

Your Committee recommends that this matter be referred to the Coos County Medical Society.

I move that this recommendation be adopted.

This motion was seconded and was carried.

DR. DUBE: The committee recommends that the House of Delegates go on record that the fee for services rendered in taking blood for the premarital blood test shall not exceed three dollars per person.

I move that this recommendation be adopted.

This motion was seconded and was carried.

DR. DUBE: Regarding the Wagner Act the committee recommends that the following resolution be adopted:

WHEREAS, the Wagner Bill (Senate Bill 1620) of the Seventy-Sixth Congress, entitled the National Health Act, in Title V, Part 1, pertaining to maternal and child welfare, gives the Children's Bureau of the Labor Department (1) broad powers in imposing rules and regulations for the states; (2) undefined and indefinite advisory councils for the participating states; (3) authority for expending $63,000,000 in three years and an unlimited sum thereafter; and

WHEREAS, to the same bureau is delegated the authority to expend $73,000,000 in three years and an unlimited sum thereafter for medical services for children and services for crippled and other physically handicapped children without regard to their ability to be cared for by private funds and with an indefinite and undefined advisory council; and

WHEREAS, in Title XII, entitled Grants to States for Hospitals and Health Centers, there is provision for constructing such institutions within three years to the amount of $158,000,000, with the provision that the state participating will give reasonable assurances of continuing maintenance of added hospitals, and that these hospitals shall be available to all groups of the population, and that there is no provision in the act for determining the needs for such facilities; and

WHEREAS, the existing hospital facilities are for the most part adequate, and approximately 30 per cent of the bed capacity is not utilized, and in this act there is no provision for grants of money to these hospitals, privately owned, that for years have been carrying the burden of hospitalization; and

WHEREAS, the taxpayers residing in more advanced and progressive states, where efficient hospitalization is provided by private agencies, will be required to assist in paying for new hospital facilities in more backward states; and

WHEREAS, under Title XIII, entitled Grants to States for Medical Care, there is appropriated $35,000,000 for the first year and an unlimited sum thereafter, "to extend and improve medical care, including all services and supplies necessary for the prevention, diagnosis and treatment of illness and disability," with no provision for distinction between medical care for the indigent and that for self-sustaining persons, except to stress care for those in "severe economic distress"; and

WHEREAS, financial participation in the provisions of this bill, by the State of New Hampshire, would increase the state taxes, or there would be necessary a curtailment or discontinuance of many activities and public benefits in order to obtain the money to meet the federal grant; and

WHEREAS, the implications and interpretations of the bill, with reference to compulsory health insurance under governmental bureau supervision, are not clear; therefore, be it

RESOLVED, by the New Hampshire Medical Society, That the provisions embodied in Senate Bill 1620 are vague, wasteful, and present no definite plan, and with the use of federal and state funds would set up government hospitals and a vast indefinite system of medical care that might in the end undermine and drive out of existence

all private and church hospitals and the private practice of medicine; and, be it further

RESOLVED, That the secretary of the Society shall send copies of this resolution to the members of Congress from New Hampshire and also to the following senators: Senator Elbert D. Thomas, of Utah, chairman of the Senate Committee on Education and Labor, and the members of the subcommittee having this bill in charge, namely James E. Murray, of Montana, Vic Donahey, of Ohio, Allen J. Ellender, of Louisiana, Robert M. LaFollette, Jr., of Wisconsin, and Robert A. Taft, of Ohio, and shall request these members to obtain modification of this bill, in accordance with the previously declared policies of the American Medical Association and, in the event of failure in this effort, to oppose the act.

DR. DUBE: I move the adoption of this resolution.

This motion was seconded and was carried.

DR. DUBE: The Farm Security Administration program has been accepted by Grafton, Sullivan and Cheshire counties.

DR. SYCAMORE: I move that the House of Delegates approve in principle the proposals of the Federal Farm Security Administration, the details to be worked out by the Committee on Medical Economics with power to act with the participating county societies.

The motion was seconded. On a roll call, twelve voted no and seven yes. The motion was not carried.

DR. DUBE: We have a letter from the American Committee on Maternal Welfare, Inc. They want the House of Delegates to approve the showing of the picture, "The Birth of a Baby," which was given last year at the annual meeting.

Your committee recommends that the House of Delegates go on record as approving the exhibition of the film, "The Birth of a Baby," subject to the provisions written in the contract relative to the distribution of the picture.

This motion was seconded and was carried.

DR. DUBE: I have a letter from the Department of Public Welfare, relative to its medical plans.

Your committee recommends:

1. The establishing of the General Medical Advisory Committee to the Department of Public Welfare and that this general committee be broken down into two subcommittees: Medical Advisory Committee on General Medical Care and Medical Advisory Committee on Eye Conditions.

2. That the membership of the Medical Advisory Committee on General Medical Care is to consist of Drs. Graves, of Concord, Bowler, of Hanover, and Joyce, of Nashua.

3. That the membership of the Medical Advisory Committee on Eye Conditions is to consist, for one year, of Drs. Hunter, of Dover, Nutter and Marcotte, of Nashua, Coyle, of Hanover, Togus, of Manchester, and Ingalls, of Berlin.

4. That the president and secretary of the Society serve as ex-officio members of the General Medical Advisory Committee.

5. That the General Medical Advisory Committee shall designate each year the members who shall serve on the subcommittee on eye conditions.

I move the adoption of this recommendation.

This motion was seconded and was carried.

DR. DUBE: I have a letter from the Council on Industrial Health of the American Medical Association, relative to the possibility of the formation of a Committee on Industrial Health in the New Hampshire Medical Society.

The committee feels that no such committee should be formed because the State already has a Commission on Industrial Health, composed of three labor men, three manufacturers and three doctors.

I also have a communication from the American Medical Association, Bureau of Legal Medicine and Legislation, regarding the construction of a new building for the Army Medical Library and Museum, in Washington.

The Seventy-Sixth Congress passed an act to construct this building, but they failed to appropriate the money this year.

The committee feels that it has no recommendation to make.

DR. DUBE: Lastly, I have a letter relative to the United States Employees' Compensation Commission for the distribution of medical services to WPA workers.

The committee recommends that no action be taken and that an injured employee be allowed to choose his own doctor.

This motion was seconded and was carried.

SPEAKER DYE: Is there further new business? If not, a motion is in order to adjourn.

DR. DUBE: I move that we adjourn, until 8:30 tomorrow morning.

This motion was seconded and was carried.

Whereupon, the second meeting of the House of Delegates was adjourned at 10:20.

* * *

The House of Delegates convened at the Hotel Carpenter, Manchester, on Friday morning, June 9, 1939, at 8:30, with Speaker W. J. Paul Dye, of Wolfeboro, presiding.

The following members answered the roll call:

The President, ex-officio
The Secretary-Treasurer, ex-officio

Chester L. Smart, Laconia
A. Philip La France, Laconia
Francis J. C. Dube, Center Ossipee
Edgar J. Thibodeau, Berlin
Leslie K. Sycamore, Hanover
Deering G. Smith, Nashua
George C. Wilkins, Manchester
Clarence E. Dunbar, Manchester
George V. Fiske, Manchester
Henry O. Smith, Hudson
Wendell P. Clare, Portsmouth
John A. Hunter, Dover

SPEAKER DYE: We are ready to take up new business.

DR. COBURN: We voted yesterday to formulate plans for the one hundred and fiftieth anniversary of the Society.

I appoint the following committee for that purpose: Henry O. Smith, chairman, Fred E. Clow and Carleton R. Metcalf.

DR. SMITH: It has been suggested that the retiring president be a member of that committee. I should like to make it a committee of five, with the vice-president elect added to the list, as well as the retiring president.

This motion was seconded and was carried.

SPEAKER DYE: Is there further new business?

DR. COBURN: The Women's Auxiliary would like to have the sanction of the Society in their efforts to sell *Hygeia*.

I move that the House of Delegates favor the project.

This motion was seconded and was carried.

SPEAKER DYE: We will now have the report of the Nominating Committee.

Report of Nominating Committee

OFFICERS

President: James B. Woodman, Robert W. Holmes, John A. Hunter.

Vice-President: Ezra A. Jones, Henry C. Sanders, Jr., Ralph W. Tuttle.

Councilors: John J. Brosnahan, Cheshire County; Emery M. Fitch, Sullivan County.

Trustee: Henry O. Smith.

Speaker: Fred Fernald.

Vice-Speaker: Robert O. Blood.

Delegate (American Medical Association): Deering G. Smith.

Alternate Delegate (American Medical Association): Emery M. Fitch.

Necrologist: Henry H. Amsden.

COMMITTEES

Amendments to Constitution and By-laws: Fred E. Clow, Philip McQuesten, Louis W. Flanders.

Control of Cancer: George C. Wilkins, Howard N. Kingsford, George F. Dwinell.

Medical Economics: Leslie K. Sycamore, Richard W. Robinson, Clarence E. Dunbar.

Medical Education and Hospitals: John P. Bowler, James W. Jameson, Herbert L. Taylor.

Mental and Social Hygiene: Charles H. Dolloff, Benjamin W. Baker, John B. McKenna.

Public Relations: President, Vice-President, Secretary-Treasurer, Robert J. Graves, John F. Holmes.

Publication: Carleton R. Metcalf, Warren H. Butterfield, Ellsworth M. Tracy.

Scientific Work: Carleton R. Metcalf, Frederick P. Scribner, Nathan T. Milliken.

Tuberculosis: Robert B. Kerr, Robert M. Deming, John D. Spring.

Advisory Committee on Medical Relief: Robert J. Graves, John P. Bowler, Roland J. Joyce.

Child Health: Colin C. Stewart, Jr., Travis P. Burroughs, Franklin N. Rogers.

Maternity and Infancy: Robert O. Blood, Benjamin P. Burpee, Marion Fairfield.

SPEAKER DYE: You will vote by ballot for president.

Voting by ballot for the office of president then took place.

DR. DUNBAR: The total number of votes cast was 15, all for James B. Woodman.

SPEAKER DYE: Dr. Woodman has just been unanimously elected president of the Society for the coming year.

You will now vote by ballot for vice-president.

Voting by ballot for the office of vice-president then took place.

DR. DUNBAR: The total number of votes cast was 16; Dr. Sanders received 3, Dr. Tuttle 4, and Dr. Jones 9.

SPEAKER DYE: Dr. Jones has been elected vice-president of the Society for the coming year.

You have heard the further report of the Nominating Committee. What is your pleasure?

DR. DUBE: I move that the Secretary cast one ballot for the remainder of the slate.

This motion was seconded and was carried.

SECRETARY METCALF: I move that we express our gratitude to the Manchester medical group for the work which they have done this year and the courtesy they have shown in inviting us to come again.

This motion was seconded and was carried.

DR. CLARE: I move that we adjourn.

This motion was seconded and was carried.

Whereupon, the 1939 meeting of the House of Delegates was adjourned at 9:15.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 25351

PRESENTATION OF CASE

A twenty-nine-year-old white married Italian woman was admitted complaining of amenorrhea and hirsutism.

At the age of eighteen years the patient noted a sudden cessation of menses following a thirty-day period of almost constant flow. The amenorrhea lasted until the time of admission. Her menstruation began at the age of thirteen years and was normal and regular until the age of eighteen. She continued to have slight cramps and a "warm feeling" at the time of the expected period up until the time of entry. There were no further complaints until two years prior to admission. She was married four years after the onset of the amenorrhea. Two years before entry she began developing a beard followed by the growth of hair on the chest, arms, legs and abdomen. Five months before admission she began to notice the loss of hair from the scalp and a receding hairline on the forehead. There were no pigment changes in the skin, no striae and no unusual change in the size of the abdomen. As a young girl she weighed 100 pounds, at the time of marriage 140 pounds, one year before admission 170 pounds. She then dieted and reduced to 140 pounds in two months. On entry she weighed 146 pounds. Since childhood she had had a fainting spell once every few months but these were never related to her catamenia. Following one of these three months before entry she saw a physician who referred her to the Out Patient Department. A sugar tolerance test two months before entry showed the following curve: 67, 129, 127, 118, 98 and 50 mg. per 100 cc. Plain x-ray films of the abdomen and skull showed no visible abnormality. There had been no loss of libido and no personality change. No voice changes were noted. She had not had headaches but had noticed blurring of vision after reading for a while.

She had been constipated most of her life and used mild cathartics almost daily. On two occasions in the past year she had noticed red blood in the stools which she thought came from hemorrhoids. There were no urinary symptoms. She had not been pregnant. At the age of eighteen years, shortly after the onset of the amenorrhea, an abdominal operation was performed which revealed no cause for the condition. She was told that she had an acute appendix. Following this she had two subcutaneous injections weekly for a year without result. She had eleven brothers and sisters all of whom were normal except one obese sister aged twenty-five years who had never menstruated but showed no evidence of hirsutism.

Physical examination showed marked hirsutism with frontal alopecia and long dark hair over the chin, trunk, arms and legs. The skin and mucous membranes were normal. The patient had a contralto voice. Examination of the eyes was negative. The thyroid was negative. The breasts were atrophic and masculine in type. The heart and lungs were negative. The blood pressure was 90 systolic, 60 diastolic. The abdomen was negative. The clitoris was moderately enlarged. The vagina was essentially normal. The cervix was negative except for a few small cysts. The uterus was of normal size and freely movable. In the left vault the ovary was palpable and apparently contained a 1.5-cm. rounded nodule. There seemed to be some induration in the right uterosacral ligament.

The urine examination was negative except for an occasional red or white cell. The blood showed a red-cell count of 5,100,000 with 100 per cent hemoglobin, and a white-cell count of 12,000 with 80 per cent polymorphonuclears. A blood Hinton test was negative. The total serum cholesterol was 166 mg. per cent. Two androgen assays on twenty-four hour specimens of urine yielded values of 8.5 and 6.3 mg. (method of Callow).

On the fifth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. CHARLES H. LAWRENCE:* This story puts us at once in doubtful territory because the causes of masculinization are many, and there are some marked cases of hirsutism for which we can find no adequate explanation. I think we must assume that the patient's amenorrhea and hirsutism were due to a common factor, though it is possible, but highly improbable, that they may have been due to different factors. It was a permanent amenorrhea.

In discussing the possible causes of this condition, there is no series of cases of hirsutism or amenorrhea large enough to give us any very definite statistical background. It is interesting that in one group, that of the adrenal tumors, the majority of the patients begin to menstruate at an early age, between ten and eleven. This patient began at thirteen, a perfectly normal age. She

*Assistant professor of medicine, Tufts College Medical School; chief of Endocrine Clinic, Boston Dispensary.

had no complaints until two years before she came in. "Two years before entry she began to develop a beard followed by the growth of hair on the chest, arms, legs and abdomen." That apparently means there was some endocrine disturbance at that time.

Women with such growth of hair are a serious problem because the condition creates a profound psychologic trauma. I know one case where the patient committed suicide because of the development of a marked beard. These patients want something done right away. One has to be careful not to be overcome by the patient's anxiety for immediate therapy and jump at a conclusion without sufficient evidence.

Starting with the symptom hirsutism there are two large groups, one with associated endocrine disturbance and another in which so far we have been unable to find any endocrine dysfunction. There are four endocrinopathies which develop hirsutism, and often changes of secondary sex characteristics are associated: arrhenoblastoma, tumor of the adrenal cortex, the so-called Cushing's disease, and the "oat-cell" tumor of the thymus. I have never seen a case of "oat-cell" tumor, and they are very scarce in the literature. All these masculinizing endocrinopathies are scarce of course, but the thymic type is the least common of all. In reading the various accounts of these patients in the literature and looking for any straw that might tell the direction of the wind, I have been struck by the fact that loss of hair and receding hairline are more frequently reported in patients said to have arrhenoblastoma, than they are in those with Cushing's syndrome or tumors of the adrenal cortex. In this history we note the statement: "Five months before admission she began to notice the loss of hair from the scalp and a receding hairline on the forehead."

There was no pigment change in the skin. All of us have in the back of our minds the association of pigmentation of the skin with disease of the adrenal glands, but one can see either Addison's disease or tumor of the adrenal cortex without pigmentation, so that this does not help one way or another.

There were no striae. I should say that would be rather against the idea that this was a case of Cushing's disease, but not entirely, because in the subsequent history a possible explanation occurs and that is that she had gained a lot of weight and then lost it. She gained from 100 pounds as a girl and 140 at the time of her marriage — it is an interesting psychological problem that every woman "weighs in" at marriage — to 170 and then reduced to 140; she weighed 146 pounds when she came in. In other words, she gained some 70 pounds over her weight as a girl and 30 over what she weighed at marriage and then succeeded in getting rid of most of it. The weight of Cushing's disease is hard to reduce by diet.

We come now to the blood sugar curve. It and the fainting suggest the possibility of hypoglycemic attacks, but I do not believe one can prove them. The sugar-tolerance fasting level was 67 mg., with a peak of 129 and a final figure of 50. The last is certainly a low figure, and if it went to 50 mg. on that test it may have been lower at other times and may have accounted for the fainting attacks, but that is pure speculation. The curve is important, however, because in the majority of patients with Cushing's basophilism the curve is reversed and takes the character of the so-called diabetic curve. So this is a definite piece of evidence against Cushing's disease.

"There had been no loss of libido." I do not know whether we can rely on that, but again it fits better with arrhenoblastoma than with Cushing's disease. The patients with Cushing's disease that I have known have had definite loss of libido.

The blurring of vision suggests something wrong in the skull, but it is nothing more than suggestive.

"On two occasions in the past year she had noticed red blood in the stools which she thought came from hemorrhoids." I should be inclined to agree with her. In a young woman such bleeding might be perfectly well accounted for by hemorrhoids, and it seems to me we have no reason for indulging our imaginations and speculating about malignant disease of the ovaries that had spread to the rectum or something of that sort.

The fact that eleven years ago the abdomen was opened and nothing found does not necessarily mean there was nothing there because these masculinizing tumors can be extremely small and yet exert profound effects on sex characteristics. If the tumor happens to be in the cortex of an adrenal gland I am sure it would be impossible to rule it out by transperitoneal palpation.

In the family history we find that she had eleven brothers and sisters who were normal and one sister aged twenty-five who was obese and who had never menstruated. There is slight evidence that in this particular family perhaps endocrine dysfunction was in the inheritance, and that is all you can say about it.

"The skin and mucous membranes were normal." If that is true it is quite valuable evidence against Cushing's disease, because one of the striking findings in this disease is the almost

constant rounding of the face and reddening of the skin so that the patient suggests a full moon rising in the evening of a hot day in summer. The features are plethoric, the face very round, and the skin is a deep red and looks as if when pricked with a needle the blood would spurt.

"The patient had a contralto voice." I am not sure if the examiner was hedging or not. The characteristic voice change in adrenal cortex hyperfunction is a change to the masculine voice. It is not a question of soprano or contralto, but one of whether it is base or baritone. The quality of the voice is different, not just the pitch, so I think we must say that she did not have masculinization of the voice.

"The breasts were atrophic and masculine in type." That is definite masculinization, and peculiarly enough I think atrophy of the breast has been reported more often with arrhenoblastoma than in Cushing's disease, but not more often than with adenomas of the adrenal cortex.

"The blood pressure was 90 systolic, 60 diastolic." Certainly there was no hypertension, but there have been a number of patients reported with adrenal cortex tumor who never developed hypertension.

"The clitoris was moderately enlarged." We again have evidence of masculinization. So we have besides the hirsutism, two important physical signs of masculinization, the atrophied breasts and the hypertrophied clitoris. We might jump off the deep end and say that this was an arrhenoblastoma, but I do not want to jump.

"In the left vault the ovary was palpable and apparently contained a 1.5-cm. rounded nodule." It is rather intriguing to suggest that we have malignancy of the ovary here and some involvement of the uterosacral ligament, but I think we are not quite justified in making that a hard and fast conclusion.

The red-cell count is higher certainly than the normal average among women, and of course one of the characteristic findings of Cushing's disease is an increase in the red-cell count and hemoglobin. This again sways us over to the possibility of a Cushing tumor.

There was no significant increase in the androgen. In the last patient with adrenal tumor that I had, we measured the hormone by the capon unit and it was about ten times the normal male level. There was no question about it — you could tell which bird was the injected and which the control across a large room. On the other hand one sees masculinization associated both with adrenal tumor and with arrhenoblastoma without increase in male sex hormone. I think the level of hormone production must fluctuate from time to time.

There is one thing that I should like very much to know. It is not given here; that is, whether the bones, particularly the spine, showed demineralization.

Dr. Felix Fleischner: None of the bones showed evidence of decalcification.

Dr. Lawrence: One of the outstanding features in Cushing's disease is kyphosis of the spine, which comes on early and is due to decalcification.

Where then do we stand? The "oat-cell" tumor of the thymus I am going to throw out on the basis of its extreme rarity. The lack of characteristic changes in appearance, the lack of hypertension, the lack of demineralization and the lack of any spinal kyphosis make me think that Cushing's disease is the least probable of the remaining three possibilities and that this girl probably had either an adrenal cortical tumor or an arrhenoblastoma. The character of the hair loss on the head, the lack of high blood pressure despite years of symptoms and the lack of loss of libido incline me to think that this was more probably arrhenoblastoma than it was a tumor of the adrenal cortex.

Dr. Fuller Albright: I think if the person who prepared the clinical abstract had seen the patient a few other points would have been emphasized. She had marked virilism aside from the hirsutism — notably broad shoulders, and a quite large clitoris. In Cushing's disease you never get real virilism, rather hirsutism without other evidence of virilism. That is also true of some adrenal tumors — those associated with Cushing's disease. The absence of a decreased sugar tolerance was strong evidence against an adrenal tumor. The differential I considered was between arrhenoblastoma and nothing, and I rather favored nothing. We see in the Out Patient Department many women with hirsutism and somewhat large clitorises in whom nothing is found at operation; in fact, that is our usual experience. The amenorrhea, of course, was suggestive of arrhenoblastoma. We were disappointed to find that the sterone assays were normal, and I think they were correct. I know of nothing in the literature on any other assays in arrhenoblastoma cases.

Dr. Joe V. Meigs: Our preoperative diagnosis was arrhenoblastoma. At operation both ovaries were found to be abnormal but the right one contained a sizable tumor. This ovary was removed in toto, and a small tumor which proved to be a simple fibroma was resected from the left ovary.

Clinical Diagnosis

Arrhenoblastoma of the ovary.

Dr. Lawrence's Diagnosis

Arrhenoblastoma of the ovary.

Anatomical Diagnosis

Arrhenoblastoma (adenoma tubulare testiculare type) of the ovary.

Pathological Discussion

Dr. Benjamin Castleman: Except for a thin rim of normal ovarian tissue, the right ovary was composed of a firm yellowish tumor measuring 5 by 3 by 3 cm. Grossly it resembled the so-called xanthofibroma of the ovary. Histologically the tumor consisted of well-formed tubules quite characteristic of the adenoma tubulare testiculare, first described by Pick[1] in 1905 and now believed to be the most differentiated type of arrhenoblastoma. Readily recognizable on purely histological grounds, these tumors do not necessarily produce masculinization.

With a fat stain, however, we were able to find the so-called Leydig or interstitial cells that apparently produce the male hormone and which should be present in active arrhenoblastomas. The correlation of morphology and physiology in these ovarian tumors is intriguing but often unsatisfactory. Meyer[2] and Schiller[3] have encouraged us to believe that such correlation is usually possible. Norris,[4] on the other hand, suggests that the term arrhenoblastoma being derived from "arrhenos" meaning male, should be used only for those tumors with masculinizing effects; that is, it should be a physiological not a morphological diagnosis. Our own experience in the field is limited. We have seen masculinization relieved by oophorectomy where the ovarian tumor failed entirely to show the characteristic picture of arrhenoblastoma described by Meyer. We have also seen morphologically typical arrhenoblastomas without masculinization.

The small fibroma removed from the other ovary showed no unusual features and was merely incidental.

Dr. Albright: It is interesting that, in spite of the fact that we did not get an excess of sterone or male hormone, one month after the operation she had a menstrual period and has had regular periods since.

Dr. Meigs: How about the hirsutism?

Dr. Albright: She said that before operation it was progressively getting worse but that now it has failed to change. She also has developed pain in the breasts and has lost weight.

Dr. Meigs: Is it not possible that some of these tumors have periods when they are active and produce symptomatic effects and others when they are quiescent?

Dr. Albright: The ovary had not ceased function here because it produced amenorrhea, and as soon as the tumor was removed, her menses returned.

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CASE 25352

Presentation of Case

First Admission. A seventy-seven-year-old man was admitted complaining of urinary retention.

For many years before admission the patient suffered from gradually progressing frequency of urination, cloudy urine and increasing difficulty in emptying the bladder. There had been no hematuria or other symptoms referable to the genitourinary system. Also for many years he had had attacks of precordial pain with exertion.

Physical examination revealed a well appearing man. The tongue was clean, and the chest clear. The heart was slightly enlarged with a moderate apical systolic murmur, a regular pulse of 84, and a blood pressure of 180 systolic, 80 diastolic. Examination of the abdomen was negative except for the presence of a moderately sized right inguinal hernia and a small left hydrocele. The right and left testes were normal in size and consistence. Rectal examination revealed a moderately large, soft symmetrical prostate. The residual urine was 500 cc.

The urine examinations showed a specific gravity which ranged from 1.004 to 1.016, with + to ++ albumin and a sediment containing 1 to 25 red cells and 25 to 150 white cells per high-power field. The blood showed a red-cell count of 4,400,000 with 75 per cent hemoglobin, and a white-cell count of 11,000 with 88 per cent polymorphonuclears. Urine cultures showed *Bacillus pyocyaneus* and *Bacillus coli.*

A flat abdominal x-ray film showed no evidence of stone. There were proliferative changes about the margins of the bodies of the vertebrae. The walls of the pelvic arteries showed considerable calcification, and the bones of the pelvis were very irregular at the site of muscle attachments. An intravenous pyelogram showed incomplete filling on both sides and there was little dye seen in the bladder although the patient was under observation for forty-five minutes. The pelves were not dilated, and the ureters, so far as could be made out, appeared normal. A cystogram showed the wall of

the bladder to be very irregular, with the presence of diverticula and incomplete emptying of the organ.

The temperature was 99.6°F., the pulse 62, and the respirations 18.

A transurethral prostatic resection was performed. The vas deferens on each side was cut and ligated before operation. Two moderately sized diverticula were observed in the bladder. He had an uneventful postoperative hospital stay and was discharged on the twenty-third day.

Second Admission (two years and seven months later). Following the transurethral resection the patient was well. His cardiac symptoms improved considerably, and he led an active life. Three months before entry he noted that there was some swelling on the right side of the scrotum. This was tapped by a physician and an ounce of clear, straw-colored fluid withdrawn. Shortly after this he noted that the right testicle was sore and distinctly swollen.

On physical examination the right testicle felt somewhat irregular and was twice its normal size. Blood and urine studies were unchanged from the first admission.

The temperature, pulse and respirations were normal. A chest x-ray plate was essentially negative. A prolan A test was positive.

On the second hospital day an operation was performed.

Differential Diagnosis

Dr. J. Dellinger Barney: The first admission provides a fairly typical history of urinary obstruction, probably a prostatic obstruction. The history of precordial pain strongly suggests angina although it may possibly have been something else.

This man of seventy-seven presented not an uncommon set of physical findings. He had moderate hypertension. Inguinal hernia is not uncommon in individuals with extensive urinary obstruction, whether prostatic or due to stricture of the urethra. Also, a small hydrocele is not uncommon in people of that age, but in view of what follows it is important. It states, "The right and left testes were normal in size and consistence." They do not make it clear whether they mean the testes and epididymes or the testes alone.

Examination of the prostate showed a benign type of adenomatous hypertrophy. The result of the urine examination is what you not infrequently see in a patient with prostatic obstruction, or for that matter in any form of urinary obstruction, namely a few red cells and quite a few white cells, in other words, evidence of infection. The blood apparently was normal. The cultures, in my experience, were quite unusual. *Bacillus pyocyaneus* may have been contamination; the colon bacillus, of course, is the usual finding.

Proliferative changes of the spine are common in a man of seventy-seven and are usually due to hypertrophic arthritis. The findings in the pelvic arteries are not uncommon, in fact they are very common if a patient has arteriosclerosis. The incomplete filling of the pelvis shows that there was poor renal function. We are not enlightened as to the blood non-protein nitrogen or the phthalein test of kidney function, but the intravenous pyelogram is in itself a good test for kidney function and apparently shows a low kidney function at that particular time. The bladder on cystogram undoubtedly showed very extensive and fairly marked trabeculation, probably with sacculation and diverticulation, all of which goes with long-standing back pressure.

The temperature, pulse and respirations were not remarkable.

The division and ligation of the vas deferens is practically a routine procedure. The diverticula you might say are unimportant; very rarely do they cause much trouble, especially when the bladder is not opened. A transurethral prostatectomy was done, and he apparently made a good convalescence.

The improvement of cardiac symptoms may have been due to less activity, although it is said that he continued to lead an active life. He had a fairly long rest in bed and perhaps received other treatment for the anginal condition.

"Three months before entry he noted that there was some swelling on the right side of the scrotum." Remember on that side he had a hernia and the testicle was normal. The onset of this swelling was apparently not an acute affair but more or less gradual. There is no mention of pain or tenderness. There is no history of trauma. The tapping of the scrotum by a physician with the withdrawal of an ounce of fluid might mean that he did not get it all. There were perhaps several ounces. It is difficult to tap a scrotum with only an ounce of fluid without doing damage to the testicle. Even in experienced hands it is difficult. The layer of fluid between the testicle and the hydrocele sac is very thin, and the needle can easily damage the testicle. Shortly after that he noticed that the testicle was sore and definitely swollen.

Apparently there is no question that the right scrotum was enlarged, in fact the testicle was about twice normal size. It apparently felt irregular, a finding which suggests that the swelling was not merely an accumulation of fluid in the tunica but a mass either in the testis or the epididymis.

Dr. Tracy B. Mallory: Perhaps you can help with that description, Dr. Colby?

Dr. Fletcher H. Colby: The enlargement was definitely one of the testis.

Dr. Barney: Dr. Colby says it was a swelling of the testicle itself, which is distinctly helpful. After all the interesting and important feature of this case is the second admission. He was getting along all right until three months before he came in and then noticed that the right scrotum was swollen. It was tapped and one ounce of fluid withdrawn. Shortly after that testicular swelling was noted. Various things occur to one as possibilities. One has to consider very seriously the idea of hematocele or hematoma, a collection of blood due to tapping; for reasons I have just explained it is very easy even in experienced hands to damage the testicle when removing a small amount of hydrocele fluid. He had no fever and no mention is made of any marked amount of pain, although the scrotum was quite tender when palpated right after the tapping. That would practically eliminate any acute infection, such as a gonococcal infection, a *Bacillus coli* infection or one due to any other organism except the tubercle bacillus. It is very rare indeed to get tuberculosis of the epididymis or testicle in a man of this age; however, it does occur, and I have seen it in men over eighty. Also, it seems possible that some note would have been made of thickening of the epididymis or testicle at the time of the first operation. Gumma would seem to be eliminated by the negative Hinton test. So it is not likely that he had an infection.

He had a hydrocele, because the doctor tapped it and got some hydrocele fluid. It is well known that hydrocele will recur. It may be that this swelling was due to a recurring hydrocele; these may increase in size quite rapidly, oftentimes without any reason that we can find. A hydrocele sac might be irregular in shape and contour if it were constricted at some point.

Of course we cannot get away from the idea of neoplasm. He was not seen for two years and seven months following the first admission and during that time a neoplasm would have had time to develop. Neoplasm in the testicle in a man of seventy, however, is uncommon; we see it chiefly in patients below fifty. The fact that he had a positive prolan A is of some importance. He had had a vasectomy, however, and I believe it is not uncommon to get a positive prolan A test after vasectomy and prostatectomy. No mention is made of the number of prolan A units. He might have developed a lymphoblastoma of the testicle. This type of tumor is apt to develop rapidly late in life, and it could give this picture.

We can rule out acute things such as torsion of the testicle or of the hydatid of Morgagni. There was no pain or fever. We have been told that this enlargement was apparently that of the testicle, but palpation of the scrotum is difficult at times. It might have been the hernia that had come down. For the sake of being complete, another possibility is spermatocele. Such a condition, however, usually appears in the upper pole of the epididymis.

It seems to me that the best possibility is that he had a hematocele, with the tunica vaginalis filled with blood clot, and as the next bet I should put in neoplasm of the testis, probably a lymphoblastoma.

Dr. Colby: If you knew that this mass had definitely increased in size in the last month, as it had under my observation, would that make you change your mind?

Dr. Barney: You mean that the increase in size followed the tapping?

Dr. Colby: No. From the time the testicle was first examined by me after it had been tapped until just before operation it very definitely grew larger.

Dr. Barney: Well in that case I would rearrange the order of my diagnoses. I still would put hydrocele or hematocele quite near the top.

Dr. Colby: I operated on the patient not knowing what the diagnosis was and suspecting a neoplasm because of the feeling of the testicle and its consistence, which Dr. Barney had no way of determining, and because I knew that this mass had very definitely increased in size during the previous month. I did not know about the positive prolan test until after operation, but I do not believe that it would have made any difference in making up my mind because the patient was over seventy. I do not know how common it is for men as old as that to have a positive test, but my impression is that it is not too common.

The tumor was removed by ligating the cord and taking the testicle and right scrotal contents out en masse. On section the testicle was perhaps two and a half times as large as a normal testicle.

Clinical Diagnosis

Neoplasm of testis?
Hematocele?

Dr. Barney's Diagnosis

Hematocele?
Neoplasm, probably lymphoblastoma?

Anatomical Diagnosis

Lymphoblastoma of the testis.

Pathological Discussion

Dr. Mallory: This testicle was of a rather unusual appearance. Dr. Colby was unable to restrain his curiosity in the operating room and sliced it across himself. It looked a good deal like tumor and yet not entirely like tumor. One could still make out some slight traces of testicular architecture. He brought it over to us, and we could not make up our minds in gross what it was. When the sections came through it was obvious that it was a lymphoblastoma. It was very characteristic, and I think there can be no doubt about the diagnosis. The patient has since been looked over very thoroughly for the possibility of any other focus of disease and nothing has been found. At the present time it appears that the process was localized to the testicle.

Dr. George G. Smith: A lymphoblastoma is the same as a lymphosarcoma?

Dr. Mallory: Yes; we use the two terms more or less interchangeably to signify a tumor of which the type cell is a lymphocyte, in this case a rather undifferentiated lymphoblast.

Dr. Barney: May I ask Dr. Colby the preoperative diagnosis?

Dr Colby: I was in doubt. I thought your suggestion of hematocele was a good one. Dr. Smith also saw the patient, and he felt more strongly than I did that this was neoplasm.

Dr. Smith: I was very definitely of the opinion that the enlarged body that you could feel was the testicle itself. I did a transillumination and saw just a little fluid around the testicle; such a finding rules out hematoma quite well, and I could not figure out anything else that would account for the very definite enlargement of the testicle. He had not had fever or tenderness, which would rule out an inflammatory process. I thought tumor was the only thing it could be. I had the prolan A test done. It was not quantitative, and I think it had no value.

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THE NEW FOOD, DRUG AND COSMETIC LEGISLATION

Law and Contemporary Problems, published by the School of Law of Duke University at Durham, North Carolina, devoted one hundred and seventy-eight pages in its last Winter Number to the above general title, with authoritative papers by such authors as: David P. Cavers, professor in Duke University School of Law; Ralph F. Fuchs, professor in Washington University School of Law; Frederic P. Lee, professor in Georgetown University Law School; Milton Handler, associate professor in Columbia University School of Law; James F. Hoge, of New York City, counsel for the Proprietary Association; Robert W. Austin, member of the Committee on Federal Legislation of the New York State Bar Association; Louise G. Baldwin, first vice-president in charge of legislation, National League of Women Voters; Florence Kirlin, congressional secretary, National League of Women Voters; Saul Nelson, senior economist, Bureau of Labor Statistics, United States Department of Labor; and Ole Salthe, consultant to the Food and Drug Administration, United States Department of Agriculture. Authoritatively they have discussed such subjects as the legislative history and substantive provisions of the act of 1938, formulation and review of regulation, enforcement provision of the act, control of false advertising, appraisal from the point of view of the drug and cosmetic industries, the legislation and the food industry, a consumer's appraisal, and representation of consumers' interest in federal and state legislation and its administration.

In these discussions there is general agreement that the 1938 legislation with admitted defects represents a great advance in the control of foods, drugs and cosmetics in the interest of the consumers of them and that the control of their advertisement is the portion of the legislation seemingly least satisfactory. Says Professor Cavers: "Putting the advertising issue to one side and resolving favorably such doubts as the procedural and regulatory provisions inspire, I am convinced that the new law represents a vast improvement over the old one."

Those most concerned in bettering the old legislation made a determined effort to place advertising under the Food and Drug Administration of the United States Department of Agriculture, but the manufacturers concerned succeeded in placing it under the Federal Trade Commission but not, however, without inserting important restrictive features, not wanted by the producer and advertising interests but needed if any improvement in advertising methods could be expected. Says Professor Cavers:

> While I think the results which the Food and Drug Administration could have achieved, if it has been been vested with advertising control, may easily be exaggerated, that very fact renders me all the more pessimistic as to the possibility of Federal Trade Commission regulation, sanctioned as it is by penalties of little deterrent value and vested in a body whose record is far more distinguished in other branches of its

jurisdiction than in the control of food, drug and cosmetic advertising.

Associate Professor Milton Handler adds:

> While the Wheeler–Lea Act represents a sincere attempt to stem the avalanche of false and misleading advertising, it is no more than a first, and unfortunately inadequate, step in that direction. Unless buttressed by clarifying amendments broadening its prohibitions and implementing it with effective sanctions, it will not affect an abiding solution of the vexing problems of false and misleading advertising.

Consumer appraisal is expressed by Baldwin and Kirlin as follows:

> Passage of a bill is not the end of citizen interest in it. It should be the beginning of a new responsibility, for to be effective a law needs sound administration and active citizen co-operation. The potentialities of the law under consideration here will be fully realized only if the consumer and the enforcing agency take full advantage of it. A great deal of the protection afforded consumers is in the information that will be given them in label declarations. If consumers do not read labels and fail to make their selection of purchases on the information given there, much of the value of the law will be lost. Continuing interest in promulgation of regulations is also an important responsibility of the consumer.
>
> The Food and Drug Administration views the law as essentially a measure to protect the public and can probably be counted upon to the extent of its capacity to interpret the law in those instances requiring amplification by regulation to the advantage of the consumer. It has given remarkable service to the public in the past in spite of the handicaps of a deficient law and woefully inadequate appropriations. If Congress fails to increase the appropriations available for enforcement commensurate with the increased responsibilities under the act, the consumer will be penalized.
>
> There are weaknesses in the law unquestionably. How serious these are will only be determined after a period of enforcement. With the aroused interest of consumers, it should be possible to secure perfecting amendments as need becomes evident.

These new laws are complicated; many of the requirements of the act went into effect prior to June 25, 1939, but a new bill extends the labeling provisions and those concerning coal-tar colors to January 1, 1940, and the Secretary of Agriculture has been authorized to postpone the effective date of some of the other regulations until July 1, 1940. Time will show defects and strong places; many legal decisions must come from the courts to make clear the intent and mechanism of numerous clauses in the new law. In due season will come the time for probable changes in the legislation. It took five years and one day to get the present legislation through Congress.

To quote further:

> Perhaps the most striking characteristic of the history of the Food, Drug and Cosmetic Act is the fact that this measure, which was of consequence to the health and pocketbook of every citizen of the country and which importantly affected industries whose annual produce totals roughly ten billion dollars, never became the object of widespread public attention, much less of informed public interest. The affected industries were kept posted by their associations and their journals; some national women's organizations sought to apprise their membership of major developments; but the public at large, including persons ordinarily well-informed on national affairs, knew little or nothing of what was transpiring in Congress. I suspect that today only a small fraction of the public knows that a new law has been enacted.
>
> For the existence of this situation, the nation's press must stand primarily accountable. In the long history of the bill, the *New York Times* seems to have seen fit to give it front-page mention on but a single occasion and then only to report a disturbance in the Senate galleries. The *Times'* policy was not exceptional. The only newspapers of consequence to give consistent support to the measure were the *St. Louis Post–Dispatch*, the *Christian Science Monitor* and William Allen White's *Emporia Gazette*. Magazines of large circulation were silent or unfriendly, an attitude contrasting sharply with their militant advocacy of the Act of 1906. That this policy was due in no small degree to the fact that the measure was widely represented as menacing to advertising revenues seems inescapable.
>
> . . . . The drive to restrict the power to make multiple seizures was led by the Proprietary Association. Especially prominent in this effort of the Association were representatives of the Vick Chemical Company, of North Carolina, but that company's objective was shared by many other large concerns, among them the Lambert Pharmacal Company, of Missouri, the maker of Listerine. It was perhaps not surprising, therefore, that Senators Bailey, of North Carolina, and Clark, of Missouri, both members of the Committee on Commerce and able debaters, should enter the lists on behalf of their industrial constituents to engage in the familiar and congenial task of combatting bureaucracy.
>
> . . . . Undoubtedly there was at the outset a widespread, if not universal, preference among the affected industries for the Federal Trade Commission's continuation as supervisor of advertising. But as modifi-

> cations were introduced into the food and drug bills' advertising provisions, more and more of the leading food and drug advertisers — and publishers as well — came to the conclusion that effective control of the black sheep of the industries could be had only through Food and Drug Administration action. Possibly, therefore, the issue would not have been forced but for the vigilance of the Federal Trade Commission, which manifested a lively disinclination to see another governmental agency share its jurisdiction. In industry ranks the Federal Trade Commission found potent support among the proprietary drug manufacturers; the Proprietary Association and its smaller brethren, the United Medicine Manufacturers of America and the Institute of Medicine Manufacturers, all worked in its behalf. The principal congressional champions of the Federal Trade Commission were Senator Clark, of Missouri, and Chairman Clarence F. Lea (California) of the House Committee on Interstate and Foreign Commerce.

Without Senator Copeland's persistence no reasonably satisfactory legislation probably could have been put through. Unfortunately he did not live long after its passage to receive the deserved thanks of the people. Representatives Chapman, of Kentucky, and Mapes, of Michigan, did yeoman service for this legislation toward the end. Secretary Wallace and President Roosevelt were of great aid. Women's organizations were active and effective supporters. The unfortunate deaths from Elixir Sulfanilamide aroused widespread interest and helped toward the passage of needed legislation, in particular that related to the control of the distribution of new drugs until the safety of their administration has been proved. Alas the medical profession did little to help, even so far as pure drugs were concerned, as shown by the following from Professor Cavers:

> However, no appearance was made on behalf of the American Medical Association, its representatives merely filing a brief complaining of the rule-making powers conferred on the Secretary [of Agriculture]. . . . Dr. Woodward from the American Medical Association in his appearance denied a prevalent charge that the American Medical Association had written the bill or was a moving force behind it and then corroborated that statement by the tepidity of his support of the measure.

Individual physicians were found by the author of this editorial very willing to help by writing letters to senators and representatives; why organized medicine, as the American Medical Association likes to call itself, was so indifferent in support of legislation for pure foods, pure drugs and pure cosmetics is hard to understand.

In the future, efforts will undoubtedly be made to weaken the legislation so far passed, and this must be guarded against; improvement in it may be required by amendments or new legislation. Time will be needed for court decisions to clarify the enactments. New principles of law seem involved in this legislation. How well the Federal Trade Commission will function remains to be seen; its attitude will determine whether advertising of foods, drugs and cosmetics will come within needed bounds. Here lies the greatest uncertainty as to this new legislation. If it does not work, then the fight for more effective legislation must be begun. If this becomes necessary, it is hoped that the medical profession, by organizational and individual effort, will band with the women to fight for still purer foods, drugs and cosmetics and for more honest and less harmful advertising of them in print and by radio. Eventually these ends must be accomplished.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., *Secretary*
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INVERSION OF THE UTERUS

Mrs. L. P., a thirty-year-old woman, was admitted to the hospital three days post partum, February 5, 1931. Delivery of her fourth baby had been effected at another institution following an uneventful pregnancy and labor. The placenta had failed to separate and manual removal had been attempted with resultant inversion of the uterus accompanied by severe hemorrhage. Supportive therapy was instituted for three days and on the morning of admission unsuccessful attempts at replacement had been made. The patient was then transferred for operation.

The patient's family, past and recent systemic histories were noncontributory.

On admission the patient was blanched and

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

weak, with a pulse of 130 and a blood pressure of 100 systolic, 80 diastolic. The temperature was 101°F., and the respirations 20. The red-blood-cell count was 2,140,000 with a hemoglobin of 38 per cent. Examination disclosed a very foul, necrotic, inverted uterus, with an ecchymotic and edematous vulva and a perineum freshly lacerated to the anal sphincter.

Following a transfusion of 500 cc. of citrated blood, abdominal operation was undertaken under spinal novocain anesthesia. On entering the peritoneal cavity, a crater of the uterus presented, with the tubes and ovaries drawn into it; the ring was about 3 or 4 cm. in circumference. The uterus was reverted by clamping and traction, and a panhysterectomy performed. Iodoform gauze was used to drain the pelvis through the vagina. The patient stood the operation well and, following another transfusion of 500 cc. of citrated blood, was returned to bed in good condition.

The first two postoperative days were uneventful. On the third day the iodoform-gauze drain was removed; the patient was comfortable, and her general condition good. On the fifth day the red-blood-cell count was 3,700,000, and the hemoglobin 60 per cent; on this day the patient developed slight chest pains and a cough. On the seventh day the temperature reached 102° F., and the pulse 130. On the ninth day foul pus was expressed from the abdominal wound through two draining sinuses. The stay sutures were removed, and local irrigations begun. By the tenth day the temperature was normal and remained so. The wound cleaned up rapidly and the sinuses healed by granulation so that on the eighteenth day the patient was up and about and was discharged on the next day in good condition. At discharge the red-cell count was 4,170,000, and the hemoglobin 68 per cent.

Microscopic examination of the placenta showed no evidence of a placenta accreta.

Comment. The question of individual judgment always enters into the treatment of an inversion of the uterus that cannot be reduced. The operator undoubtedly felt in this case that the condition of the uterus was such that the chance of recovery was greater by hysterectomy than by any operation devised to reduce the inversion and leave the uterus in situ. There are no hard and fast rules one can lay down as to when to do a hysterectomy in these cases. It is obvious that the inversion should have been reduced at the time of its occurrence.

The postoperative course was complicated somewhat by the pus in the abdominal wound; this was not serious, and the successful end result certainly justified the procedure.

HAY FEVER AND ASTHMA*

There is nothing glamorous about a running nose or streaming eyes, and endless sneezing has never helped anyone make friends or influence people. But if you can say that your troubles are all due to allergy, you are at least an object of interest to your acquaintances. The common or garden variety of cold makes boring conversation. But a pretty case of allergy is always good for at least a small audience. And the more "tests" your doctor has made to find out just what kind of allergy you have, the better your chance of being the life of the house-party. The only trouble is that so many people are talking about their allergies that soon your sensitiveness to peanuts or face powder will be as sensational a subject as last Tuesday's weather.

In fact, some authorities claim that nearly half the hundred and thirty million people in this country have, at one time or another, shown sensitiveness to some substance. Certainly somewhere between one and sixty million of them find ragweed as welcome as poison ivy and would rather meet Frankenstein in a dark alley than play with a puppy.

What exactly are hay fever and asthma, and what in the world, you may ask, is this allergy? Both hay fever and asthma are types of allergy. And allergy is the name given to your body's strong dislike for certain things in the air, — such as animal dusts or plant pollens, — foods, — most commonly eggs, wheat or milk, — things you touch — such as poison ivy — or substances inside the body.

These reactions of the body to offensive articles may take the form of sneezing, coughing, running nose, streaming eyes, wheezing or a skin rash. When the body is sensitive only to dust, pollens or foods or to substances already within the system, such as germs, we call the disease hay fever or asthma, as the case may be.

We have not yet discovered why some people are sensitive to certain things, and others not. But, we have at least made good progress in tracking down the kind of thing that makes life miserable for the hay fever and asthma sufferer, as well as those of you with other types of allergy. Grandpa may laugh himself into a stroke if you should suggest that removing his terrier from the house might relieve his asthma, but we do know for a certainty that dogs, as well as cats, horses, cows, sheep and rabbits, explain many cases of allergy. And Cousin Elmer might suggest having your head examined if you advised him to get rid of his feather-bed to stop his hay fever, but you would still have the right idea. We know that dusts from kapok, chicken, duck, and goose feathers, silk, rugs, curtains, overstuffed furniture and similar articles give people hay fever. We know that plant and tree pollens are among the commonest offenders, especially pollens from oak, birch, maple and elm trees, ragweed and grasses. Flaxseed and cottonseed are also trouble-makers. The kinds of food which aggravate allergic persons are numerous and varied: wheat, oats, rice, rye, eggs, milk, beef, lamb, pork, sea food, fish, beans, potatoes, spinach, peanuts, celery, peas, strawberries, oranges, cantaloupes, tomatoes, chicken, mustard, chocolate and cocoanuts.

One of the interesting facts about allergy is that you often inherit the tendency to be allergic. Indeed, we doctors frown on a boy with hay fever marrying a girl who has asthma. Their children are very likely to be perfect little examples of inherited allergy. But since doctors always lose out in an argument with young love, all they can do is warn allergic parents to be on the watch for food

*A "Green Lights to Health" broadcast given by Dr. Walter S. Burrage on Wednesday, June 21, and sponsored by the Public Education Committee of the Massachusetts Medical Society and the Massachusetts Department of Public Health.

or other sensitivity in little Susie or Pete, and not to force spinach or the breakfast cereal if the child appears strongly to dislike it.

Seasonal hay fever and pollen asthma, both of which are caused by pollens, have, like straw hats, a particular season. Certain of the pollens which cause them, such as those from trees, — in New England the most common are oak, maple, birch, elm, and willow pollens, — are in the air during April and May. Grass pollens, which cause so-called "rose fever," float about during June and the first half of July. Ragweed, the chief cause of fall hay fever, fills the air from mid-August to frost.

Unfortunately, the seasonal hay-fever sufferer with ragweed sensitivity, for instance, cannot end his troubles merely by going out and digging up all the ragweed in the garden. Ragweed pollen can be carried by the wind for hundreds of miles and has been collected in airplanes thousands of feet above the earth. And the escape method of cure works only if you can take an ocean voyage, and too few of us can afford this. Many localities, especially in the mountains, have been advertised as hay-fever resorts, but actual pollen counts in these places have shown that there was little basis for such claims.

What can you do, then, if you have seasonal hay fever or pollen asthma? First of all, expose yourself as little as possible to the offending dust or pollen by keeping your windows shut at night or installing some kind of filtering machine in your bedroom or office windows. These filters cut down the amount of pollen about 95 per cent. But even so, relief is temporary and, at best, only partial. There are filters which can be inserted in the nose, and gas masks, but they are not practical.

The most successful plan is to go to the doctor and have him build up your resistance to the harmful substance by giving you injections. The doctor can, by listening to your story and making skin tests, usually find out the particular material that is causing the trouble. By injecting a solution of this material in gradually increasing amounts into your arm or leg, he may bring your resistance up to the point where it will cease to give you hay fever or asthma. These injections can be given during or before the season, or right through the year. Treatment during the season is least effective. Injections given before the season or all year round are best. Local treatment with sprays, salves and eyedrops gives only temporary and very slight relief.

Asthma and hay fever often have no relation to the season but occur at any time of year or even persist throughout the year. This type of allergy is caused by something in your surroundings — an animal, house dusts or foods — or by something wrong within your body, such as infection. The farmer who is sensitive to cows, for example, will have his hay fever or asthma as long as he is near the animals. The horse-sensitive stableboy will have asthma or hay fever whenever he works with horses. If you always sleep on a feather pillow, you will wheeze or sneeze the year round if you are allergic to feathers.

A competent doctor can help you. But you can help him, and yourself too, by doing a little preliminary investigating on your own account. If you think you have asthma or hay fever, begin right away to note the time, place and circumstances which seem to be related to your symptoms. When and where do you appear to have trouble: by day or night; indoors or outdoors; at home or where you work; everywhere in the house, or only in certain rooms; when the dog or cat is around, or even in places where there are no animals; when you eat lobster, let us say, or soft-boiled eggs?

Observing yourself carefully in this way will save you time and trouble, and give the doctor a start in solving the mystery. He will have to make tests in any case, but not so many as would be necessary if he must start from scratch and go through a list of several hundred possibilities. And, best of all, if you, yourself, can find what is troubling you, you can, to some extent, treat yourself by trying to keep away from it.

One thing your doctor can do, that you cannot, is build up your resistance to the harmful substance by giving you injections. And he can also help you keep away from the offensive substances, if keeping away from them is the treatment that is best for you.

* * *

Q. As you said yourself, allergy is still new enough and novel enough to cause a faint stir of interest around the tea table. But surely people must have been allergic since time immemorial?

A. Allergy is no older or younger than any other human ailment. In fact, as far back as 1798 doctors noticed things that suggested a peculiar capacity in some individuals to react toward certain substances harmless to others. But only since the World War has any headway been made in successfully treating such patients. And right now, a great deal of work is being done on the subject by research workers.

Q. Has this study of allergy gone far enough to produce concrete results in the way of relief for such conditions as hay fever and asthma?

A. It certainly has. Statistics show that 80 per cent of hay-fever patients are being helped, and over 50 per cent of those with asthma. This is a very encouraging record, and one which should be improved even further as we find out more about what causes allergy.

Q. Are tests the only way a doctor has of finding out what is causing your running nose or sneezing?

A. The history of the case is just as important as the tests. By history I mean your own account of the nature of the attacks and the circumstances under which they occur. The doctor is guided in his choice of tests and in his diagnosis by what you can tell him. He has to know whether your symptoms occurred during the winter or summer, whether they were associated with colds, whether they were worse when you were at work or at home. If you can tell him they were associated with colds, he has found a clue to the possible infectious nature of your difficulty. If you know your hay fever first occurred in June, he immediately thinks of grass pollen or so-called "rose fever." If you were well until around Labor Day, he can proceed on the assumption that you are probably sensitive to ragweed. What you can tell him about your environment is also of the greatest importance: whether there is a dog or cat in the house; what types of bedding you use; whether you use face powder, or work in a bakeshop. Bakers, for example, are often sensitive to wheat. These details may seem trivial, but they may actually lead to the correct diagnosis and successful treatment of your case.

Q. Do tests prove anything definite?

A. Tests are like things you read in the newspaper: you cannot believe everything. And an ounce of doubt is worth a pound of testing materials. A positive test does not always mean you are sensitive to the material used in the test. On the other hand, a patient may be sensitive to a substance which, when used in a test, produces a negative reaction. Any form of treatment based on the presence or absence of positive skin tests alone is

likely to be unsatisfactory, and may even be harmful, in that the patient's mode of living may be restricted beyond the bounds of common sense. In one case an overconscientious patient had reduced her diet to nothing but noodle soup, and another, who on the basis of positive tests was avoiding certain foods, as well as silks, would not eat away from home or go to the theatre, dances or any other public places where he would come in contact with silk. The results in this last case were unexpected — the patient developed a nervous breakdown from sheer inhibition.

Q. What would you say is the sensible approach to allergy?

A. A person who thinks he has allergy should first of all do something about it. Neglected hay fever can become asthma, and other forms of allergy can also develop into complicated illnesses. He should observe his symptoms, and if he cannot succeed in obtaining relief by cutting down his exposure to what he thinks is causing these symptoms, he should go to a qualified doctor and put himself in experienced hands. The doctor, by making sure the case is one of actual allergy, by translating the story in the terms of scientific knowledge, by making the proper tests and interpreting them correctly, can do a lot to put more sense in sensitivity.

DEATH

CHATIGNY — Beatrice A. Chatigny, M.D., of Taunton, died August 18. She was in her forty-ninth year.

Born in Boston she graduated from South Boston High School and received her degree from the Tufts College Medical School in 1913. Dr. Chatigny served her internship at the Massachusetts Homeopathic Hospital. For five years she served on the staff of the Taunton State Hospital and was on the staff of the Northampton State Hospital for one year.

She was a member of the Tufts College Medical School Honorary Medical Society, an honor bestowed last winter.

She is survived by her husband, Dr. Joseph V. Chatigny, treasurer of the Bristol North District Medical Society, two sons and a brother.

MISCELLANY

SECOND U.S.P. XI SUPPLEMENT

It has been learned that the *Second United States Pharmacopoeia XI Supplement* will be off the press in a few days, and stocks are to be shipped to the regular subagents throughout the country so that it may be released on September 1.

The *Second Supplement* includes new monographs for ascorbic acid, cyclopropane, mandelic acid, methyrosaniline chloride, nicotinic acid, purified cotton, soluble pentobarbital, sulfanilamide, surgical gut or catgut, thiamine hydrochloride, tribasic calcium phosphate, tribasic magnesium phosphate, natural vitamin A in oil, and natural vitamins A and D in oil, official for the first time. Two of these substances, tribasic calcium phosphate and methyrosaniline chloride, were in *National Formulary VI*, but these new U.S.P. standards now supersede the previous ones.

The *Second Supplement* also includes a revision of eighty-five of the monographs of the original *U.S.P. XI*, particularly the revision of antipneumococcus serum, including the recognition for the first time of Types 2, 5, 7 and 8; under tetanus antitoxin the use of animals other than the horse is permitted, while under diphtheria toxoid, the alum-precipitated form is given official recognition. It also contains a new bioassay method for thiamine hydrochloride (vitamin B_1). Improved assays for vitamin A and vitamin D are also given.

An important feature is the cumulative index which lists all U.S.P. titles and indicates where the present official monograph now in force may be found. This index emphasizes the fact that the *U.S.P. XI* now consists of three volumes — the original *U.S.P. XI*, which became official on June 1, 1936, the *First U.S.P. XI Supplement*, official December 1, 1937, and the *Second U.S.P. XI Supplement*, which will become official January 1, 1940.

In the new supplement the following exceptions are made for the revised monographs for cod-liver oil and nondestearinated cod-liver oil and for the new monograph providing standards for surgical gut or catgut. These three texts do not become official until July 1, 1940, six months additional time's being allowed for the adjustment of labels and existing stocks.

To insure prompt delivery of the supplements, orders should be sent, accompanied by a check or money order, to the General Agent, The Mack Printing Company, Easton, Pennsylvania. The price of the *First U.S.P. XI Supplement* is $1.00 prepaid, and for the *Second U.S.P. XI Supplement*, which is considerably larger, $1.50, prepaid. A substantial, spring-back cover, serving as a single binder for all U.S.P. supplements, is also available. The binder sells for $1.50.

CORRESPONDENCE

RESTORATION OF LICENSE

To the Editor: This is to inform you that in accordance with the vote of the Board of Registration in Medicine, the license of Dr. David H. Shulman revoked on August 18, 1938, was restored to him on August 21, 1939.

Stephen Rushmore, M.D., *Secretary*,
Board of Registration in Medicine.

State House,
Boston.

NOTICES

REMOVALS

Robert T. Monroe, M.D., announces the removal of his office from 721 Huntington Avenue, Boston, to 270 Commonwealth Avenue, Boston.

Edmund Myers, M.D., announces his removal to 343 Second Avenue, North, St. Petersburg, Florida.

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Monday, September 4

Tuesday, September 5

*10 a.m.–12:30 p.m. Boston Dispensary tumor clinic.

Friday, September 8

*10 a.m.–12:30 p.m. Boston Dispensary tumor clinic.

Saturday, September 9

*10 a.m.–12 m. Staff rounds of the Peter Bent Brigham Hospital. Conducted by Dr. Soma Weiss.

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*Open to the medical profession.

SEPTEMBER 5 — Dermatology and Syphilology Clinic, Lawrence General Hospital. Page 325, issue of August 24.

SEPTEMBER 4–6 — Institute for the Consideration of the Blood and Blood-Forming Organs. Page 941, issue of June 1.

SEPTEMBER 4–6 — Institute at University of Wisconsin Medical School. Page 160, issue of July 27.

SEPTEMBER 5–8 — American Congress of Physical Therapy. Hotel Pennsylvania, New York City. Page 857, issue of May 18.

SEPTEMBER 11–15 — American Congress on Obstetrics and Gynecology. Page 938, issue of December 8.

SEPTEMBER 14–16 — Biological Photographic Association. Page 941, issue of June 1.

SEPTEMBER 15–28 — Pan-Pacific Surgical Association. Page 863, issue of November 24.

SEPTEMBER 29–30 — New England Surgical Society. Beverly and Salem.

OCTOBER 23–NOVEMBER 3 — New York Academy of Medicine. Page 977, issue of June 8.

FALL, 1939 — Temperature Symposium. Page 218, issue of February 2.

DECEMBER 2 — American Board of Obstetrics and Gynecology. Page 1019, issue of June 15.

JANUARY 6, JUNE 8–11, 1940 — American Board of Obstetrics and Gynecology. Page 160, issue of July 27.

MARCH 7–9, 1940 — The New England Hospital Association. Hotel Statler, Boston.

MAY 14, 1940 — Pharmacopoeial Convention. Page 894, issue of May 25.

JUNE 7–9, 1940 — American Board of Obstetrics and Gynecology. Page 1019, issue of June 15.

BOOKS RECEIVED FOR REVIEW

Diagnosis and Management of Diseases of the Biliary Tract. R. Franklin Carter, Carl H. Greene and John R. Twiss. 432 pp. Philadelphia: Lea & Febiger, 1939. $6.50.

Treatment by Manipulation. A. G. Timbrell Fisher. 255 pp. New York: Paul B. Hoeber, Inc., 1939. $3.75.

Doctors, Nurses and Dickens. Robert D. Neely. 153 pp. Boston: The Christopher Publishing House, 1939. $1.50.

Medical Climatology: Climatic and weather influences in health and disease. Clarence A. Mills. 296 pp. Springfield, Illinois and Baltimore: Charles C Thomas, 1939. $4.50.

L'Examen du Malade: Guide clinique de l'étudiant et du médecin. P. Delmas, G. Giraud, E. Jeanbrau, E. Leenhardt, J. Margarot, P. Pages, V. Riche, L. Rimbaud, J. Terracol, H. Villard. Second edition. 365 pp. Paris: Masson et Cie, 1939. 45 Fr. fr.

Tuberculosis and Social Conditions in England: With special reference to young adults. P. D'Arcy Hart and G. Payling Wright. 165 pp. London: National Association for the Prevention of Tuberculosis. 1939. 3s.

Provoked Alimentary Hyperglycemia: The mechanism of the tolerance test. Joseph M. Flint. 37 pp. London, Ontario: A. B. Macallum, 1939.

The Effect of the Macallum–Laughton Duodenal Extract Upon Hypophyseal Diabetes. Joseph M. Flint and Louis Michaud. 77 pp. London, Qntario: A. B. Macallum, 1939.

Manual of the Diseases of the Eye: For students and general practitioners. Charles H. May. Sixteenth edition. 515 pp. Baltimore: William Wood & Co., 1939. $4.00.

Otolaryngology in General Practice. Lyman G. Richards. 352 pp. New York: The Macmillan Co., 1939. $6.00.

Surgical Applied Anatomy. Frederick Treves. Tenth edition. 748 pp. Philadelphia: Lea & Febiger, 1939. $4.50.

A Textbook of Microbiology. Kenneth L. Burdon. Second edition of *A Textbook of Bacteriology.* 638 pp. New York: The Macmillan Co., 1939. $2.75.

How to Counsel Students. E. G. Williamson. 562 pp. New York and London: McGraw–Hill Book Co., Inc., 1939. $3.75.

Teaching for Health. Marguerite M. Hussey. 328 pp. New York: Prentice–Hall, Inc., 1939. $2.25.

One Hundred Thousand Days of Illness. Dorothy Ketcham. 477 pp. Ann Arbor: Edwards Brothers, Inc., 1939. $2.10.

Sleep and Wakefulness: As alternating phases in the cycle of existence. Nathaniel Kleitman. 638 pp. Chicago: The University of Chicago Press, 1939. $5.00.

Historical Directory of State Health Departments in the United States of America. Robert G. Paterson. 68 pp. Columbus: The Ohio Public Health Association, 1939. $1.00.

Epidemic Encephalitis: Etiology, epidemiology, treatment. Third report of the Matheson Commission. 493 pp. New York: Columbia University Press, 1939. $3.00.

Treatment in General Practice: The management of some major medical disorders. Vol. 1 and 2. 695 pp. Boston: Little, Brown & Co., 1939. $7.50.

John Howard (1726–1790), Hospital and Prison Reformer: A bibliography. Leona Baumgartner. 79 pp. Baltimore: The Johns Hopkins Press, 1939. $1.00.

BOOK REVIEWS

Zur Entdeckung der Insulinschocktherapie bei akuten Geisteskrankheiten, insbesondere bei der Schizophrenie. Julius Schuster. 90 pp. Budapest: Druckerei der Pester Lloyd–Gesellschaft, 1938. 2 Pengö.

In this small book, the author first gives a chronologic survey of his studies in the shock treatment of psychoses. He shows that von Jauregg's experiments concerning the influence of injections of proteins and of pyocyaneus bacilli on non-syphilitic psychoses were the starting point for his investigations. In 1926 the author reported a new procedure for the treatment of acute mental disorders before the Royal Hungarian Medical Association in Budapest. This concerned the sedating effect of large doses of insulin, as well as the elimination of hallucinations and of various thought disturbances, which was brought about by the drug. At that time he explained that the favorable change which he noticed in his patients was due to the condition of the brain as a whole, as well as that of the entire organism. The author made detailed statements about treatment with insulin, claiming that the transformation of carbohydrates into fats and the changes involving the intermediary metabolism of the brain, conditioned by the insulin, also the compensation of the existing glycogen reserves by large intravenous doses of glucose, all had a decidedly curative effect. In addition, extensive histopathological investigations led him to believe that there were certain pathologic changes which suggested a morphological basis for schizophrenia.

The author then tries to prove that insulin-shock treatment eliminates the pathologic disturbance which he suggested as the underlying cause of schizophrenia. For that purpose he first describes the basic biochemical facts of the insulin-shock effect. He discusses the significance of the phosphatides, of the effective substances of the pituitary gland, of the growth factor and of the cortex of the adrenals. This is followed by abstracts from case records and finally is summarized as follows: "Although we could not demonstrate primary changes in the thalamus and in the nodules of the vegetative nervous system of schizophrenics and although most authors regard the changes in the thalamus and in the vegetative nervous centers as secondary phenomena that depend on changes

in the cells of the brain cortex, it cannot be doubted that in cases of schizophrenia the extreme loss of weight, the anorexia and the extreme need of water, as evidenced by polydipsia and polyphagia, to a certain extent can be regarded as cortical effects on the water center, the salt center and the sugar center." On the basis of his observations the following conclusions are drawn: "In cases of sudden confusion and amentia, insulin therapy is of deciding significance, since it shortens the course of the disease; the restlessness of the patient ceases, his instinct for nutrition awakens and artificial nourishment becomes superfluous; the mental condition of the patient changes; the confusion rapidly disappears."

The whole book appears to be a bid for priority in the treatment of the schizophrenias with large doses of insulin. It cannot be recommended as an authoritative study on insulin-shock treatment, and does not contain any valid or valuable information from a scientific or clinical point of view.

Handbook of Physiology and Biochemistry. W. D. Halliburton and R. J. S. McDowall. Thirty-fifth edition. 973 pp. Philadelphia: P. Blakiston's Sons & Co., Inc., 1937. $5.50.

Since 1848 this handbook has merited new editions from time to time. It should be noted that the title of this book now includes "biochemistry." The aim consistently has been to meet the needs of the medical student preparing for examination. Description of methods has been restricted, except in those cases of later practical value or of educational importance in directing one's attention to the fundamentals of physiological knowledge. The textual material has been brought up to date in regard to the humoral transmission of nerve impulse, enzymes, vitamins, sex hormones, lymph formation, the pituitary gland, general metabolism and diet. A special feature of the book is the consideration of how various organs co-operate in the interest of the whole organism. The book is well bound and written on good paper, and the facts are presented in a style that will appeal to students and general practitioners of medicine.

Handbook of the Vaccine Treatment of Chronic Rheumatic Diseases. Oxford Medical Publications. H. Warren Crowe. Third edition. 95 pp. New York: Oxford University Press, 1939. $1.25.

H. Warren Crowe is the director of the Charterhouse Rheumatism Clinic in London. Evidently this clinic is confined to the treatment of chronic rheumatic diseases and the principal treatment that they depend on is the use of stock vaccines of streptococci and staphylococci, which are apparently employed for all types of arthritis. He gives detailed descriptions of the use of these vaccines and many case reports.

This book is of value to anyone interested in studying vaccine treatment.

Medical Jurisprudence and Toxicology. William D. McNally. 386 pp. Philadelphia and London: W. B. Saunders Co., 1939. $3.75.

This is a frank condensation of the author's larger book on toxicology. The limitations in size of the book are accountable, as the author explains in his preface, for the elimination of many details for which the reader is referred to the larger volume. Of the total pages, 278 are given up to toxicology. In 66 pages the high spots of the subject of medical jurisprudence are touched. The book of necessity is inadequate in both fields.

The Clinical Diagnosis of Swellings. C. E. Corrigan. 313 pp. Baltimore: The Williams & Wilkins Co., 1939. $4.00.

It is well established that men who have been rigorously trained in sailing vessels without the benefit of radio compasses and mechanical depth finders make the best masters of modern ships. By the same token, the doctor who has been trained to rely on his five senses and frontal lobes in reaching a diagnosis without too much reliance on the x-ray and the laboratory is the best clinician. In this day of highly specialized mechanical, chemical and electrical aids to diagnosis, the ancient art of medicine has been somewhat neglected. It is, therefore, refreshing to encounter a volume such as this in which the diagnosis of swellings of every type in the body is considered solely from the point of view of their physical characteristics and in the light of deductive reasoning.

The presentation is simple and straightforward and greatly enhanced by excellent diagrammatic drawings. The gross pathology of swellings is emphasized over their often less clear-cut, microscopic characteristics. At the end of each chapter a tribute is paid in thumbnail sketches to the men of the past whose names are frequently associated with the subject matter. In reviewing the medical nomenclature of form, the author notes that we have no term which clearly denotes the shape of a mass or swelling formed by the segment of a sphere. He happily suggests the term hypospherical for such a mass. A large sebaceous cyst on the scalp might thus be described as hypospherical. The chapter on ulcers is particularly noteworthy, with an excellent description of the various forms of skin cancer.

Most surgeons of experience would disagree with the statement in the chapter on enlarged lymphatic nodes that such nodes are invariably fixed to the surrounding tissues when they are the seat of metastatic cancer. Also, the author's assertion that testicles in any position, abnormal or otherwise, always retain their general shape when they become the seat of disease cannot be endorsed without qualification.

This book could be read with great profit by every second-year or third-year medical student and should prove stimulating to the teacher or clinician who is interested in the art as well as the science of exact diagnosis.

Food and Health: An introduction to the science of nutrition. A. Barbara Callow. Second edition. 168 pp. Oxford: The Clarendon Press, 1938. $1.75.

Among the treatises now being placed before the profession and the public those dealing with the importance of nutrition in maintaining health are appearing in considerable numbers with the purpose of making recently acquired knowledge available for all who are disposed to take advantage of it. In this list the book by A. Barbara Callow takes high rank. Beginning with explanations of the physiologic chemistry of nutrition the reader is given explanations of the nature of the several essential elements which enter into the structure and promote the growth of the human body. The digestive processes by which these elements are utilized are described, and a chapter is devoted to the vitamins.

After laying down this scientific basis for the maintenance of a normal body, the rest of the book is devoted to the relative importance of the different foods with qualitative and quantitative proportions to be used to maintain health and cure those diseases which result from deficiencies in one or more of the elements. To those people who are obliged to consider the economic prob-

lems of feeding a family, the seventh chapter will be found especially valuable.

Many tables give detailed information which will relieve the busy housewife of having to draw conclusions from more elaborate compositions. The book is well written and devoid of confusing technical terms.

Rural Medicine: Proceedings of the conference held at Cooperstown, New York, October 7 and 8, 1938. 268 pp. Springfield, Illinois and Baltimore: Charles C Thomas, 1939. $3.50.

Much of what we do not know can be found by study and observation under conditions far simpler than those obtaining where most of the scientific time and money is spent. Sir James Mackenzie felt this to be so when he moved from Harley Street to St. Andrews twenty years ago. The personality behind the Conference on Rural Medicine held at Cooperstown in October, 1938, is not so plainly evident, but the reviewer suspects that another, more modest Mackenzie had something to do with it. Certainly the Mary Imogene Bassett Hospital, of which George M. Mackenzie is physician-in-chief, has demonstrated the feasibility of a small hospital's serving as the focus for community-health interests to a far greater degree than has been suggested heretofore. This is the greatest but by no means the only inspiring value of the present volume, which reports the papers and discussions of the Cooperstown conference.

The book divides itself into the following parts: about one hundred pages dealing with rural morbidity; about forty pages on public-health and school-health programs in rural areas; thirty pages on postgraduate medical education in rural areas; and approximately seventy pages dealing with the economics of rural medicine. There is appended a bibliography of rural medicine which lists two hundred and fifty odd publications.

Experts in many of the fields covered have contributed to the proceedings. The material is entertainingly illustrated and cast into the form of graphs and charts. The book is well made and easy to read. The outstanding feature, however, is the comprehensive approach to the problems of rural medicine. One wishes it might be given even a tithe of the publicity so freely spent on certain professional proclamations in the same domain during 1938.

Chronic Arthritis. Robert T. Monroe. Edited by Henry A. Christian. 84 pp. New York, London and Toronto: Oxford University Press, 1939. $2.00.

The author presents a simple, practical, fairly brief description of chronic arthritis based on his experience with 267 cases of atrophic arthritis and 466 cases of hypertrophic arthritis. The presentation is remarkable for its freedom from prejudice. The book should be read by all who are wondering whether their patients have atrophic or hypertrophic arthritis and by those who propose to suggest a type of treatment with which they are not familiar. Most medical interns would profit by reading the book in order to obtain a good general idea of the arthritic problem.

Syphilis and Its Accomplices in Mischief: Society, the state and the physician. George M. Katsainos. 676 pp. Athens, Greece: Privately printed, 1939. $5.00.

This work could, by a slight stretch of the imagination, be considered peculiarly characteristic of a particular spirit of these times because of its very thinly-veiled attack on the physician in his relation to the society among which he practices medicine. The very title is not only an insinuation but a slur, and one not in the best taste.

It is very difficult to classify this book; it certainly cannot profess to be a textbook for the physician nor can it have been intended to be entirely a source of information for the laity. It is, rather, a compendium: a compendium of philosophy, of a sort; Greek history; Greek mythology; a smattering of medical history; a defense of the intellectual superiority of the German race [*sic*]; a touch of sympathy for the "martyrdom of Nicholas Romanoff," and an invective against the Church and Christianity. It also contains several expressions of self-appraisal for the author's great industry and fortitude under the rebuffs of his contemporaries in the practice of medicine. It is a little difficult for this reviewer to accept such a work as the proper place for a description of an interview with Dr. John T. Bowen in the course of which the author was refused admission to serve at the Massachusetts General Hospital. Nor does it seem to be the place for such a statement as, "this country has known just three presidents who governed it according to the constitution, Jefferson, Lincoln and Theodore Roosevelt, and one absolute dictator, Wilson." There is a fairly rich supply of translations from the Greek of ancient medical writings. However, what are the exact sources? Are the translations the author's own?

There are a number of statements related to the subject of syphilis as a whole which, in the opinion of the reviewer, constitute a serious indictment of the value of this work when judged by modern standards. To quote only a few: gummata are capable of transmitting the disease "like the secondary lesions"; "Hereditary syphilis may be transmitted in three ways: 1. By double hereditary infection, at the moment [*sic*] of conception by the parents who are luetic and not under treatment. 2. By maternal transmission. . . . 3. By paternal transmission. . . ."; "Their ravages [those by syphilis and gonorrhea] can be restrained if the state, by legalizing and ennobling prostitution will teach the citizens, first, how to protect themselves properly from these diseases and, next, how to treat themselves, if once affected by them." (In other words, he recommends restoring the erstwhile profession of prostitution to the former glories which once surrounded it in ancient history.)

He says of secondary syphilis: ". . . the disease at this stage may be considered a light disease and therefore curable." Another very startling statement: "One of the principal reasons for the early manifestations of paresis and tabes dorsalis . . . is the lumbar puncture and the repeated injury and disturbance which is caused by it on the nervous system." He is apparently uncompromising in the opinion that the treatment for chronic syphilis must go on forever.

Although this voluminous work contains many very enjoyable references to Plutarch, Sophocles, Aeschylus, Hippocrates, Thucydides and other old Greek masters, it is nevertheless an excessively verbose composition of a few challengeable ideas about the clinical development of syphilis. The book is poorly printed and profusely interspersed with many typographical errors, some of which are unimportant and others very important. For instance, in describing the dose for salvarsan, he states that it ranges from "0.015 milligrams to 0.04 centigrams." The error here is only too obvious to those who use the drug. One very interesting contribution is a philological discussion of the proposal to substitute the term "syphilodogonus" for spirochete or treponeme.

Appended to this text is a reprint of a small book entitled *Marriage and Syphilis*. The author tells an interesting story of adventures in his attempts to have this book published and to have it reviewed by the press. This book is afflicted by the same heavy impediments which encumber the larger work. It also suffers from a somewhat strabismic viewpoint of the relation of the medical profession to this disease. For instance, there is the passage: "The tragedy becomes even worse if we remember that the cause of these evils [syphilis and gonorrhea] is often the physician and becomes more revolting when we consider that the physician never suffers any harm but, on the contrary, is left free to bring about many more similar disasters for the sake of a sordid gain." And again, a startling statement: "Woman as an imitator is generally capable of reproducing good work, but as a physician she is surely bankrupt and therefore she ought to be forbidden to enter the medical profession." Shades of Susan Blackstone! His concluding definition of syphilis is an index of his general theme: "a disease which . . . the medical profession deceives and plunders and which . . . cannot be defeated, conquered and consequently exterminated."

This combined volume of two books should certainly not be read by anyone who is not properly qualified to be adequately critical.

The Student's Handbook of Surgical Operations. Frederick Treves. Sixth edition, revised by Cecil P. G. Wakeley. 563 pp. New York: Paul B. Hoeber, Inc., 1939. $5.00.

This is the sixth edition and twenty-first reprinting of this deservedly popular handbook. With the shelves of libraries filled with treatises on surgery, this book remains almost unique in confining itself only to the actual technical procedures of operations. At the time of its original writing, operations on the extremities and the periphery of the body in general constituted much more of surgery than they do today. This is still reflected in the present edition. For example, much space is devoted to amputations. However, this section is admirably written. The consideration of the subsequent usefulness of the limb in relation to the site of amputation is very well emphasized. Also, much attention is paid to operations on the bones and joints, in particular, excisions of joints. Possibly a greater incidence of bone tuberculosis in the British Isles makes these procedures commoner than they are in this country. The author of this edition has restrained himself from a discussion of operative indications in general but does list the conditions which present absolute and relative indications for operations on the sympathetic nervous system; with many of these, American surgeons are likely to disagree.

The volume should continue to serve the useful purpose it has for the past forty years and undoubtedly will remain a companion piece to Treves's *Applied Anatomy* in the libraries of many surgeons.

The Control of the Circulation of the Blood. R. J. S. McDowall. With the assistance of G. E. Malcomson and I. McWhan. 619 pp. London, New York and Toronto: Longmans, Green & Co., 1938. $22.50.

This volume is an important contribution as a source or reference book for physiological and clinical observations on the control of the circulation. No original material is presented, but reviews and criticisms of work that has been done in this large field are well presented. The author discusses the control of the blood vessels, vasodilator mechanisms, blood depots, the cerebral circulation, the pulmonary circulation, the coronary circulation, the cutaneous circulation, and the hepatic and renal circulations in the first eight chapters. Then he goes on in the remainder of the book with the resting heart rate, the cardio-inhibitory mechanism, cardiac acceleration, the action of adrenaline, the control of the secretion of adrenaline and the method of its study, the action of carbon dioxide and acid-base equilibrium, the effects of general anoxemia and high altitude, asphyxia, the effects of changes of temperature, the effects of sleep and mental activity, of exercise, of posture, of hemorrhage, and of the pituitary, the hypothalamus, and the action of certain substances used in the investigation of the circulation, such as choline and acetylcholine, atropine, histamine and pancreatic extracts. There is an extensive carefully selected bibliography.

This volume can be recommended as a useful reference book to anyone — physiologist, clinical investigator or practicing physician — who is working in the field of the control of the circulation.

Textbook of Medicine. By various authors. Edited by J. J. Conybeare. Fourth edition. 1112 pp. Baltimore: The Williams & Wilkins Co., 1939. $6.75.

This is a good textbook of medicine, as evaluated by comparison with the standard work of Osler, which still ranks highest in this field. It is written by various British authors, but its editor and largest contributor J. J. Conybeare, physician to Guy's Hospital, London, has attained a high degree of unity of style, marked by clarity and conciseness. It is thoroughly abreast with recent advances in medicine, and novel features attractive to the practitioner are sections on psychological medicine, or psychiatry, and on common diseases of the skin.

From the point of view of the art of bookmaking it is excellent, being smaller, lighter and better bound than the majority of standard textbooks. It is a fourth edition and gives promise of many more to come.

You Can't Eat That! A manual and recipe book for those who suffer either acutely or mildly (and perhaps unconsciously) from food allergy. Helen Morgan. 330 pp. New York: Harcourt, Brace & Co., 1939. $2.50.

In this book the author presents scientific facts associated with the practical application of experiments tending to show that the "millions" of victims of allergy may expect relief, in a large proportion of cases, if treated by physicians who are qualified to meet the complex problems involved.

The importance of allergic reactions is emphasized in the statement that "medical science admits that simple foods may incite explosions that vary from a rash to a fatality." It is said that when the cause of an attack is found it is not enough to tell the patient that the offending food must be avoided, because substitutes must be included in the dietary of many cases in order to maintain adequate nutrition.

After an explanation of allergy in its many phases the reader is informed about its causes, and how the disease is diagnosed and treated, with a very complete history of the gradual accumulation of knowledge relating to it. The remainder of the book is devoted to the foods which are blameworthy, substitutes, methods of cooking and a voluminous list of recipes.

The book is well written, and the facts and opinions contained therein are presented in an interesting fashion. No better endorsement could be written than that presented in the foreword by Dr. Walter C. Alvarez.

A Textbook of Clinical Neurology: With an introduction to the history of neurology. Israel S. Wechsler. Fourth edition, revised. 844 pp. Philadelphia and London: W. B. Saunders Co., 1939. $7.00.

In twelve years since the first issue of this book four editions have been called for, a fact which speaks highly of its value as a textbook. In the present edition, there are a few changes made necessary by the major advances in neurology since the third edition in 1935. Unfortunately, the author has not sufficiently kept in touch with the growing literature of neurology, and the edition is not so thoroughly revised as one would expect. There are, moreover, numerous small errors in the book which should have been corrected by the fourth edition. The most serious errors are those in relation to the dosage of drugs, in one case ten times the ordinary dose being recommended. It is hoped that in future editions more attention will be paid to matters of this kind.

American Medicine Mobilizes. James Rorty. 358 pp. New York: W. W. Norton & Co., Inc., 1939. $3.00.

This book should be read by all physicians who are interested in economic problems in medicine and who are not familiar with the existing facts before they begin to consider plans for the improvement of the distribution and excellence of medical care.

The author presents in a clear and precise manner the important factors which must be realized by anyone who tackles these problems. He obviously is hostile to the attitude of organized medicine, as represented by the American Medical Association, and is perhaps rather bitter in his criticism of Dr. Morris Fishbein. On the other hand the data which he presents to substantiate his claims are convincing. He brings out clearly the points which the reports of the Committee on the Costs of Medical Care and of the American Foundation, that of the Interdepartmental Committee to Co-ordinate Health and Welfare Activities at the National Health Conference and other surveys have established. He emphasizes that the existing fee-for-service system in the practice of medicine cannot continue unless some program to provide the fee is instituted, and states that some type of prepayment insurance other than cash indemnity insurance must be the answer. He is appreciably less optimistic than the reviewer in regard to the possibility of voluntary prepayment insurance plans' developing to meet the situation and asks, since there is no doubt that compulsory health insurance by government will eventually develop, why it should not be put into effect now.

The author also brings out clearly what an indefinite line of demarcation exists between patent and so-called ethical proprietary medicines. This point has troubled many physicians for years, and the power, or perhaps evil, that powerful drug interests can exert on organized medicine by their financial support is well emphasized in the book.

The Principles and Practice of Ophthalmic Surgery. Edmund B. Spaeth. 835 pp. Philadelphia: Lea & Febiger, 1939. $10.00.

This book is evidently the fruit of a tremendous amount of work. The author not only has drawn on his own large surgical experience, but for the most part has presented the most important operations devised by others. In such a comprehensive work the descriptions are often necessarily brief, but adequate for the purpose. There is an unusually thorough treatment of plastic surgery related to the eye, doubtless on account of the author's especial interest in the subject. The chapters on retinal separation give a comprehensive review of the subject from the standpoints of etiology and operative and postoperative treatment. In general the reviewer believes that the author has stressed the best types of operation for various conditions. One must, however, regret the dismissal in a single sentence of the intracapsular extraction of cataracts as advocated by Verhoeff, that is, the combined forceps and pressure extraction, where the lens is grasped at the upper pole and brought out without tumbling. This operation has been done practically to the exclusion of all others at the Massachusetts Eye and Ear Infirmary since about 1927, and the results as reported by Grossman, Beach and others certainly compare favorably with those of other methods.

On the whole, the book admirably fulfills the long-felt need of an adequate, up-to-date text of ophthalmic surgery in English. It is a book no one doing this type of surgery can afford to be without.

The Canned Food Reference Manual. 242 pp. New York: American Can Co., 1939.

The story leading up to the publication of the new *Canned Food Reference Manual,* recently compiled by the Nutrition Laboratory of the Research Department, of the American Can Company, is an intensely interesting one. It was brought about through the realization that not only must reliable information on canned foods be made available to laymen but — equally important — more technical information on this great class of foods should be provided those professions which deal intimately with canned foods.

Consequently, in 1935, the American Can Company inaugurated its present practice of issuing each month in the journals serving the medical, dental, nursing, dietetic and home economics professions, a factual release covering in technical vein some phase of canned-food knowledge. The great demand for some type of publication which would bring all these releases together within one binding was met first by publication of *Facts About Commercially Canned Foods* in 1936, and later by issuance of *Nutritive Aspects of Canned Foods* in 1937. The present text has been prepared to amplify and extend, rather than to replace, the above prior publications.

Health for 7,500,000 People: Annual report of the Department of Health, City of New York, for 1937 and a review of developments from 1934 to 1938. John L. Rice. 390 pp. New York: Department of Health, City of New York, 1939.

This is the annual report of the Department of Health of New York City, popularized by the inclusion of nontechnical phraseology and by pictures in the best candid manner. The reviewer found much information, as one always does in such reports. The total permit fees collected by the department approach half a million dollars annually. There was but one case of botulism reported for seven million people over a period of seven years, and but two cases of pellagra. There was no smallpox for a period of five years, 1933–1937, during which time there were twenty-seven cases of leprosy. So one might continue noting the quaint details of the largest city. As usual the contributions of the public-health nurses are outstanding. The system of decentralized health units is now well established in New York City, and is being used at designated points for medical education. The book is well bound.